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# KETOGENIC DIETS IN MEDICAL NUTRITION: HERBAL AND NUTRACEUTICALS PRODUCTS UNIVERSITY OF SALERNO

## Abstracts Book

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# Abstracts Book

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## 1. Ghee (clarified butter), nutritional evaluation and its possible therapeutic use in the diet

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### Background

Ghee or clarified butter is made in many countries around the world, largely in Asia, the Middle East and Africa. Ghee is obtained by clarifying high temperature fat. His flavouris greatly influenced by the fermentation of the cream or butter and the heating processes. At room temperature it appears moderately solid. The color is yellow, with shades of lighter or more intensely golden, depending on the content of carotenoids. It is a source of nutrients for the presence of essential fatty acids, liposoluble vitamins, carotenoids and trace elements such as calcium, phosphorus and iron, and antioxidant compounds. Ghee is used in cooking and traditional medicine. Ease of digestion, absorption and food assimilation. It is also used as a skin emollient and facilitates wound healing and in the treatment of allergies and respiratory tract infections.

### Hypothesis/Purpose

In this paper, the manufacturing process, chemical composition, nutrition and possible therapeutic uses in the diet of Ghee were studied, through a systematic review of existing scientific publications.

### Study Design

Ghee, clarified butter, manufacture, flavor components, chemical composition, nutrition, therapeutic use, diet.

### Methods

Ghee is widely considered as the Indian name for clarified butterfat,usually prepared from cow's milk, buffalo milk or mixed milk (1). In the Middle East, ghee is commonly made from goat, sheep or camel milk and it is known as "*maslee*" or by some variant of the Arabic term "*samn*" (2). In Iran, it is called "*roghan*" (3).Due to the diffuse regional origin there are several definitions of ghee. According to Illingworth et al. (4), ghee can be defined as a pure clarified fat that is exclusively obtained from milk, cream or butter by application of heat for almost total removal of moisture and solid no fat to give a product a unique flavor, physical structure and texture. A recent definition of ghee is stated as a product exclusively obtained from milk, cream or butter by means of processes which result in almost total removal of water and non-fat solids, with an especially developed flavor and physical structure (5). The western world standard specifies ghee to have 96% minimum milk fat, 0.3% maximum moisture, 0, 3% maximum free fatty acids (FFA) (expressed as butyric acid), and a peroxide value (PV) less than 1,0. According to Illingworth et al. (4), worldwide, there are four methods for the production of ghee: the indigenous milk butter method, the direct cream method, the cream butter method and the pre-stratification method. The quality of ghee is determined by three parameters: Peroxide value, Flavour and Acidity. The temperature of clarification is most important factors that control the intensity of flavour of ghee. Ghee prepared around 110°C has somewhat mild flavour. Flavour retains longer if ghee contains 1% NaCl. The flavour of ghee is affected by the acidity of cream or butter. Cream butter having acidity of 0.15-0.25% produces a ghee with most acceptable flavour (6).The highly prized characteristic flavour of ghee is due to a complex mixture of compounds produced during the various stages of processing. Carbonyls (aldehydes and ketones), lactones (7), free fatty acids (8),esters (9) and miscellaneous substances (10) are reported to be the key ghee flavouring compounds (7). Ghee is

complex lipids of glycerides, free fatty acids, phospholipids, sterols, sterol esters, liposoluble vitamins (A, D, E and K), carbonyls, hydrocarbons and carotenoids. Ghee also contains traces of iron, phosphorus and calcium. The major constituent of ghee is glycerides which constitutes 98% of total material in ghee and rest 2% consist of sterols most commonly cholesterol (0, 3-0, 4%) (11). About 70% of the fatty acids present in the starting milk are saturated, including 60% of the long chain (12). Among the most important are the conjugated linoleic acid (CLA), present in high concentrations. The acronym CLA refers to a mixture of the conjugated positional and geometric isomers of linoleic acid (cis-9, cis-12 octadecadienoic acid) (13). During the manufacture of ghee, milk protein provides hydrogen, which reacts with the double bonds of linoleic acid during heating under anaerobic conditions and catalyzes the formation of CLAs, similar to the microbial enzymatic reaction in the rumen (14).Ghee lipids contain not only saturated fatty acids to an extent of approximately 60% of total fatty acids but also contain approximately 0.15 to 0.30% cholesterol. Cholesterol in food materials undergoes oxidation during processing, resulting in the formation of cholesterol oxidation products (COPS). Studies in the literature show that concentrations in COPS ghee vary from 0.7 to 0.9% of total cholesterol (15).

## Results

The relationship between food and health has long been known to exist, and today the fundamental concept of food is changing from one involving the maintenance of life to one maintaining and promoting better health and quality of life by preventing chronic diseases. For example, hypercholesterolemia, obesity and oxidation stress are the major risk factors that accelerate the development of cardiovascular diseases and the progression of atherosclerosis (14). Based on this, several experiments were carried out in Wistar rats, which demonstrated the antioxidant effect of enzyme enriched enzyme conjugated linoleic acid and its antiaterogenic, anti-cancerous, anti-diabetic and anti-adipogenic properties (14).Ghee in diets is a rich source of energy since it has a high caloric value. It's an important ingredient since it consists of some essential acids and antioxidants as: glutathione, vitamin C, A and E which react with oxidants (free radicals) in the cell cytosol and in the blood protect the cell thanks to all 'help with enzymes such as: catalase, superoxide dismutase and peroxidase (16). In its presence, the COPs were only produced when the ghee was used for frying for a long time (11).Ghee contains high levels of saturated fatty acids and cholesterol, which are considered risk factors for cardiovascular diseases (17).Cholesterol in food materials undergoes oxidation during processing, resulting in the formation of cholesterol oxidation products (COPS), which are reported to be atherogenic, mutagenic, cytotoxic, and angiotoxic (18). Nath et al. (1996) showed that ghee manufactured and stored under normal conditions did not contain COPS. They were formed only when the samples underwent auto-oxidation to such an extent that they became unacceptable for consumption. The findings in literature with experimental animals do not give any support for linking ghee consumption to hypercholesterolemia and hyperlipidemia, which are considered to be risk factors for heart diseases (17).Moreover, in the indigenous Ayurvedic system of medicine, ghee is used in the preparation of a number of formulations for treating allergy, skin, and respiratory diseases and is considered to induce many beneficial effects on human health (19-20).

## Conclusion

Through a systematic review of existing scientific publications, manufacture process, physical and chemical characteristics, nutrition, advantages and quality of ghee were studied.Ghee is an important constituent of Indian meal. It is prepared using different methods. By definition, ghee is a product exclusively obtained from milk, cream or butter by means of processes that involve the almost total removal of water and non-fat solids, with a particularly well developed taste and physical structure. Further research is needed to clarify the net effect of ghee due to the presence of both COPS and CLAs that may have both negative and positive effects. Given the various unique characteristicschemical,

nutritional, the manufacturing process and usage, ghee will continue to be a product of social and economic importance in these countries.

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## 2. Flaxseed Oil: Composition, Nutritional and Therapeutic Role. A Possibile Implication in Metabolic Syndrome

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### Background

Flaxseeds (Linumusitatissimum in using L.) are cultivated mainly for the extraction of an oil (about 38-45%) containing about 40-50% ofα-linolenic acid (ALA), a good amount of phytosterols, mainly β-sitosterol, campesterol andstigmasterol , and tocopherols,which have an important therapeutic activity.

### Hypothesis

The announced study project has focused on assessing the possible effects of flaxseed oil on metabolic syndrome

### Study Design

The study was dealt with on multiple levels, or rather considering the effects of flaxseed oil on individual pathological cases that are the basis of metabolic syndrome: hypertension, hyperlipidemia, insulin resistance, subdivided respectively into CASE 1, CASE 2 and CASE 3.A review has been carried out on the various works published in the literature over the last few years.

### Methods

In CASE 1, they were examined studies in which humanssupplemented their habitual diet with flaxseed or its extracts (i.e., oil, lignans, fiber) for ≥2 week.

In CASE 2 a randomized, double blind, crossover study, was evaluated. 15 subjects ingested 10 g of flaxseed oil (FO) or corn oil (CO), containing 5.49 g and 0.09 g of ALA, respectively, once daily with dinner. Blood samples were collected at 0, 4 and 12 weeks, and were used for analysis of serum lipid, lipid-related proteins, serum fatty acids and serum sd-LDL cholesterol.

For the CASE 3 a randomized crossover design was considered. Nine obese glucose intolerant people consumed 40 g ground flaxseed or 40 g wheat bran daily for 12 weeks with a 4-week washout period. Plasma inflammation biomarkers (CRP, TNF-α, and IL-6), glucose, insulin, and thiobaribituric acid reactive substance (TBARS) were measured before and after of each supplementation.

### Results

A total of 11 studies (14 trials) were included in the analysis of CASE 1. Results indicated that flaxseed supplementation reduced systolic blood pressure (−1.77 mm Hg)and diastolic blood pressure (−1.58 mm Hg). These results were not influenced by categorization of participants into higher baseline blood pressure (≥130 mm Hg).

The results of CASE 2 suggested that FO supplementation was associated with a significant decrease in sd-LDL concentrations at 4 and 12 weeks, and CO supplementation had no effect. Moreover, sd-LDL concentrations were significantly lower in the FO period than in the CO period at 4 weeks. Among subjects

with triglyceride (TG) concentrations of >100 mg/dl, FO supplementation markedly reduced sd-LDL concentrations at 4 and 12 weeks compared with baseline.
The results of CASE 3 showed that flaxseed supplementation decreased TBARS ($p = 0.0215$) and HOMA-IR ($p = 0.0382$). Flaxseed or wheat bran supplementation did not change plasma inflammatory biomarkers. A positive relationship was found between TBARS and HOMA-IR ($r = 0.62$, $p = 0.0003$).

**Conclusion**

Flaxseed therapy can be used as an adjuvant with diet and medicines in management of various metabolic derangements of metabolic syndrome. Such studies should be further encouraged as medicinal herbs constitute the corner stone of traditional medicinal practice worldwide. Such studies should be ideally done for a longer duration and large population group to know the changes of BMI and WHR.

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## 3. Influence of medium-chain triglyceride (MCT) of coconut oils on cholesterol metabolism and related disorders

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### Background

Functional foods, "those foods that encompass potentially healthful products including any modified food or ingredient that may provide a health benefit beyond the traditional nutrients it contains", have been suggested to provide benefits for weight management via decreased lipid storage and uptake, enhanced rates of fat oxidation, and increased satiety One functional food that has been proposed to act on both energy expenditure and energy intake is medium chain triglycerides (*MCT*). *MCT* bypass chylomicron incorporation for lymphatic transportation, providing the liver with a ready supply of energy and reducing peripheral fat deposition into adipose tissue .In humans, MCT consumption enhances reductions in adiposity. Structure lipids with a MCT backbone and linoleic acid built into the triglyceride molecule have been developed to optimize the triglyceride structure that is best for patients, particularly the critically ill. Developing countries are undergoing rapid nutrition transition concurrent with increases in obesity, the metabolic syndrome, and type 2 diabetes mellitus (*T2DM*).

### Hypothesis/Purpose

Recent years have brought a renewed interest in lipids and their role in the metabolic and dietetic applications in health care of hospitalized patients as well as the public at large. In the search for alternative noncarbohydrate fuels, medium chain triglycerides (*MCT*) are unique and have established themselves in the areas of malabsorption syndrome cases and infant care and as a high energy, rapidly available fuel.Coconut oil has an unusually high amount of medium-chain triglycerides (MCTs). These are harder for the body to convert into stored fat, and easier to burn off than long-chain triglycerides (LCTs). Like other saturated fats, it is solid when at room temperature and liquefies when heated.In baking, coconut oil gives a light, sweet, "*coconutty*" flavor. It substitutes well for butter and shortening in recipes, and works well as a plant-based replacement for vegan recipes.

### Methods

A total of 14 studies were analyzed, of which 7 evaluated satiety, 8 assessed body composition and 6assessed the energy expenditure (EE). Only one study (7%) found a positive effect on satiety, 6 (43%) found apositive effect on body composition and 4(29%) found a positive effect on EE, with the use of MCT.The study was conducted with eutrophic individuals, who consumed the majority of MCT in mealswhen compared to those who also examined satiety.Studies evaluating the effect of MCT on body composition showed a positive effect related to the body mass index (*BMI*) of the participants. Of the 6 studies inwhich this effect was observed, most were performedwith overweight or obese individuals (*BMI*< 25 kg/m2).Of the four studies in which the positive effect on the EE was observed, two showed a positive correlation with body composition, both being performed in over-weight individuals.The studies shown in the table indicate that the posi-tive effect on body composition and EE resultant of MCT intake occurs after at least 4 weeks of consump-tion. this effect, at least on body composition, is only reallysignificant in the first two weeks of consumption, thus suggesting a possible metabolic adaptation. Moreover, bolus ingestion of MCTs

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tends to trigger thermogenesis, presumably reflecting the fact that a glut of acetyl-coenzyme A production in mitochondria tends to trigger protective uncoupling mechanisms-

**Results**

Not all coconut oils are the same, and some are more healthful than others. Partially hydrogenated coconut oil is just as harmful as other highly processed oils that contain trans fats. These are not healthful. Refined coconut oil is extracted from chemically bleached and deodorized coconut meat.Virgin coconut oil is extracted from the fruit of fresh, mature coconuts without using high temperatures or chemicals. It is considered unrefined, and it may offer health benefits. Coconut oil contains 2.6 percent fewer calories than other fats. It has been said to provide various health benefits:

1. increasing "good" cholesterol: a component in coconut oil has been found to give "good" HDL cholesterol "a nudge."
2. Controlling blood sugar: it appears to preserve insulin action and insulin resistance in mice.
3. Reducing stress: It has antistress and antioxidant properties, which could make it useful as an antidepressant, according to research in rodents.
4. Shiny hair: It makes hair shinier, because it penetrates better than mineral oils.
5. Healthy skin: it has been found to enhance protective barrier functions and have an anti-inflammatory effect on skin in humans.
6. Preventing liver disease: it has reversed hepatosteatosis, a type of fatty liver disease, in rodents.
7. Reducing asthma symptoms: Inhaling coconut oil has helped reduce asthma symptoms in rabbits.
8. Fighting candida: Coconut oil has reduced colonization with Candida albicans in mice, suggesting it could be a treatment for candida.
9. Improving satiety
10. Weight loss: It has reduced obesity and promoted weight loss in mice.

This abstract aims to provide evidence from the scientific literature that coconut oil should be classified as a medium-chain saturated fat, since its fatty acid composition is over 65% *MCFA*. Coconut oil is a unique vegetable oil because it is the only oil where about 50% of the fatty acid composition is C12. Thermogenesis is linked to weight loss and is therefore considered to be a mechanism for the prevention of obesity *MCFAs* were potent *UCP1* activators, also called thermogenin, dissipates the proton motive force that is normally used to drive the synthesis of cellular ATP and the energy is released instead in the form of heat. The thermogenic ability of *BAT* is due to the uncoupling protein 1. that specializes in burning fat. *BAT* is brown because of the high concentration of iron-containing mitochondria. Brown adipose tissue (BAT) is currently implicated in the regulation of energy balance. In cold-adapted rats, hypertrophy and hyperplasia of *BAT* occur. Basal and norepinephrine (*NE*)-stimulated oxygen uptakes of coldadapted rats increase to a great extent above the values for warm-acclimated control. This dramatic increase in nonshivering thermogenesis has been attributed to the activity of *BAT* and its unique capacity to uncouple oxidative phosphorylation leading to production of energy as heat rather than as *ATP*. The evidence for *BAT (brown adipose tissue)* as the site for nonshivering the *MCT* increases energy expenditure, gives faster satiety, and facilitates weight control when included in the diet as a replacement for *LCT* fats. *MCFAs* have potential beneficial use against diabetes. Many of the properties of coconut oil can be accounted for by the properties of lauric acid. Lauric acid makes up approximately half of the fatty acids in coconut oil; likewise, medium-chain triglycerides which contain lauric acid account for approximately half of all triacylglycerides in coconut oil. It is, therefore, justified to classify coconut oil as a medium-chain vegetable oil. Dietary medium chain triglycerides (*MCT*),

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## 4. Alkaline bicarbonate waters. use in ketogenic terapie

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Ketogenic therapy is a diet that induces in the body the formation of defined ketone-like substances such as beta-hydroxybutyrate, acetic acid, acetone. Production of ketones occurs when a very low or no amount of sugars is taken, for example in fasting or very fat-rich diets. In this case, the organism and the brain, in particular, use ketone bodies as a source of energy. Salt's content in natural waters essentially depends, both quantitatively and qualitatively, on the chemical composition and on the physico-chemical properties of the rock formations with which water comes into contact and the duration of the contact itself. The source of Lete® water is located in the municipality of Pratella (CE) in the mountain range of the Matese, in the same region is realized the entire hydrogeological cycle of the mineral water fountain, from the charging area to the mineralization processes and to the underground outflow towards The source of the low valley of River Lete [1]

Studies in literature have shown that Lete water has particular chemical-physical characteristics for the presence of calcium (310 mg / l), magnesium (15 mg / l), sodium (4.9 mg / l) and bicarbonate (1010 mg / L), facilitating the hydration state [2,3].

The study is aimed at verifying the absorption of Acqua Lete®, VS Acqua Sant'Anna® into ketogenic therapy.

They were enlisted 10 N° patients in 2 heterogeneous groups in 21 days of treatment, one treatment with calcium bicarbonate water (Acqua Lete®) and the second with natural oligomineral water (Acqua Sant'Anna®), the expected water intake was at least 2 L Group, then control parameters such as urinary pH, and pH salivation, electrolytes such as sodium, potassium, chlorine, magnesium and calcium were taken into account, clinical parameters such as blood pressure, heart rate, and finally some symptoms Such as alopecia, headache, palpitations, meteorism, tiredness, muscle aches, cramps.

**Keywords**: Acqua Lete®, Acqua Sant'Anna®, Ketogenic therapy

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## 5:6. Ashwagandha, Composition and Food Conduct Management

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### Background

Ashwagandha or Withania Somnifera (Fam. Solanaceae), commonly known as "Indian Ginseng", is one of the most widely used plants for thousands of years in Indian Ayurvedic Medicine as Rasayana.
Leaves, seeds and especially roots of this shrub are used and more than 35 medicinalchemicals of it have been identified. The main ones are: alkaloids, steroid lactones and saponins.
The most important steroid lactones are: Witaferina A and Witaferina D (1).
Ashwagandha has lots of benefits, but the most important ones are the adaptogen and antistress (1, 2).
This plant is used in prevention and treatment of many diseases in which pathogenesis stress plays a significant role (arteriosclerosis, premature aging, arthritis, diabetes, hypertension, depression, overweight and obesity).
Stress causes systemic increase of hormones, such as cortisol, which can lead to changes in eating behavior, increased visceral adiposity, metabolic syndrome (7, 8, 9) and gaining body weight.

### Hypothesis:

The aim of this work is to examine studies that have shown that by taking this plant, stress is reduced, cortisol levels decrease and food behaviors of those individuals who show to be attracted to certain food or who eat disorderly can improve.
It is supposed that this plant can have enormous potential in eating behavior management.

### Study designe:

studies' review, by researching published on PUBMED, SCOPUS and GOOGLE SCHOLAR.

### Methods:

Several studies have been examinated.
One of these is that realized by Choudhary D, Bhattacharyya S, Joshi K (4), in which 56 individuals between 18 and 60 years old were chronically affected. The individuals of this study group received 300 mg standard Ashwagandha root extract twice a day for eight weeks; those individuals in the control group received placebo capsules twice a day.
At the beginning and end of the study these individuals were submitted to clinical examinations and stress assessment questionnaires.
Another similar study, which lasts 60 days, with the same active substance dosage, was realized by K. Chandrasekhar, Jyoti Kapoor e. Anishetty (5), who recruited 64 adults with a chronic stress background.
A group of authors, M.A. Pratte, Kaushal B. Nanavati, Virginia Young, Christopher P. Morley (6) also realized a review in 2014, mentioning 5 studies (7, 8, 9, 5, 10) which have the aim to test the efficacy of Ayurvedic plant on chronic stress:

Bhattacharya SK et al (11) experienced the effects of Ashwagandha on rats exposed to chronic stress. The effects were compared to those obtained by synthesis ansiolitics intaking.

**Results**

At the end of each study, the level of cortisol in blood was reduced, stress resistance increased and general well-being improved with resulting eating behavior improvement, body weight and BMI reduction.

In all studies no negative effects were observed.

**Conclusion:**

All mentioned studies show that by taking standardized Ashwagandha root extracts, stress and anxiety can be reduced, and so eating behavior can improve.

Adaptogenic power of this plant could be used in food therapies as an **adjuvant treatment**to handle psychological components related to a wrong food behavior.

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## 7. SHBG e ipofertilità, il ruolo della sindrome metabolica e dell'insulino resistenza

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### Background

Infertility affects approximately 15% of all couples. Male factors contribute to approximately half of these cases, with no identifiable cause in 25 %[1]. 'Male factor' infertility is seen as an alteration in sperm concentration and/or motility and/or morphology in at least one sample of two sperm analyses, collected between 1 and 4 weeks apart[2].Some factors such as obesity, insulin resistance, inflammatory background, radiation, smoking, varicocele, infection, urinary tract infection, environmental factors, nutritional deficiencies and oxidative stress are negatively correlated with spermatogenesis and contribute to male infertility[3].
Recently, the pivotal role that lifestyle factors play in the development of infertility has generated a considerable amount of interest. Lifestyle factors are the modifiable habits and ways of life that can greatly influence overall health and well-being, including fertility[4].

### Hypothesis/Purpose

A lot of study demonstrate that weight loss could improve a fertility race in woman also in which of them have a PCOS syndrome or a insulin resistance (IR) [5]. The link between infertility and insulin resistance is probably the inflammatory background associated with adipose tissue, particularly the visceral one (visceral fat), which is Insulin dependent. IR drastically reduces availability of sex steroids through lesser production of sex hormone binding globulin (SHBG)[6].

### Results

The results of several studies point to an increased likelihood of abnormal semen parameters among overweight men, and an elevated risk for subfertility among couples in which the male partner is obese. Obesity is, therefore, associated with a higher incidence of male factor infertility[7].

In contrast, Khaw and Barrett-Conner examined the opposite relation of sex hormones to obesity, studying baseline endogenous sex hormones as predictors of central adiposity. They found that total testosterone and SHBG were inversely related to central adiposity assessed 12 years later. The authors suggested that these results were consistent with evidence that in males, testosterone may mobilize abdominal fat deposits, and with data from studies of testosterone administration in castrated rats[8].

A VLCKD (Very low calorie Ketogenic Diet) induces an important decrease of fat mass in android level, associated with the decrease in waist circumference. G. Merra et al. Found also that whey proteins seem to cause a reduction of glycemia and a reduction of insulin resistance too[9]. and can be use also as a chance for man with low SHBG, endocrine disorder, central adipose fat, insulin residence , and infertility.

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- Male fertility (race, incidence)
- Insulin resistance, glucose tolerance and SHBG concentration
- PCOS in woman and in man
- Short time diet could improve fertility race, ketogenic diet is suggest?

## 8. Vitamin D and insulin resistance: action mechanism. The role of ketogenic diet.

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### Background
The increasing incidence of diabetes, characterised by insulin resistance, is a important problem with consequent devasting. Several life style may play a role in this rapid increase diabetes. Several clinical intervention studies support that ketogenic diet and 25-hydroxyvitamin D (25 (OH) D) improves insulin sensivity.

### Hypothesis/Purpose
This reviewsummarized the literature related to potential reduction in insulin resistance in subjects following a ketogenic diet whit simultaneous 25 (OH) D supplementation.

### Study/Design
Several studies have been cross-examined to demonstrate the importance of ketogenic diet and vitamin D in insulin resistance, but there are no references to simultaneous administration of 25 (OH) D and ketogenic diet.

### Methods
The studies considered used different methods of analysis. Both men and women were evaluated, different age groups, but also with different habits and lifestyles.The populations considered were either supplemented with 25 (OH) D or followed a ketogenic diet.

### Results
Available prospective studies show a high 25 (OH) D protective effect concentration on the risk of type 2 diabetes mellitus. There is currently a strong inconsistency in the results of vitamin D administration on secretion and insulin sensitivity, probably due to differences in the population concerned, duration of interventions and forms of integration of vitamin D.Several studies show, however, the close relationship between insulin resistance and ketogenic diet.

### Conclusion
The diversity of the methodologies used, the optimum dosage regimens of vitamin D and the optimal therapeutic concentrations of 25 (OH) D serum limit the available intervention studies. Well-designed, placebo-controlled, randomized intervention studies are required to establish a true protective influence of vitamin D on glucose homeostasis.
Instead, the strong relationship between resistance insulin and ketogenic diet is strongly confirmed today. This makes us suppose a hypothetical relationship between vitamin D supplementation, ketogenic diet and insulin regulation.

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## 9. Collagen: ultrasound eveluation at the skin and joint. Sarcopenia: Ultrasound framing

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### Background

Collagen is a fibroblast protein synthesized by fibroblasts, with remarkable tensile strength in the intercellular substance.
It helps preserve the robustness, texture and elasticity of the skin and joints.
Sarcopenia corresponds to an onset of muscle mass loss that manifests itself as a result of a long period of physical inactivity and the onset of age.

### Purpose

The aim of the study was the research, evaluation of collagen at the skin, subcutaneous and articular level by ultrasound and elastoecographic analysis.
For sarcopenic research, an ultrasonography was performed by measuring the "penning angle"

### Study design

Case study studies

### Methods

Patients were subjected to ultrasound analysis at the skin. They were invited to lie on a cot in the back.
After cleaning the probe and disinfecting it with a non-toxic substance, the operator applied the gel to the area of interest to see the thickness of the dermis, its ecogenicity and SLEB (Derma papillary).
Subsequently, they underwent an ultrasound analysis at the articular level to analyze the main component: Cartilage lalina.
*Ultrasonography:* the elasticity of the dermis and the Subepidermal Low Echogenic Band (SLEB), is the superficial dermis (papillary dermis) hypoechoic line due to the elastosis process (basophilic collagen degradation).
Ultrasound was performed at the knee level by high-frequency linear probe, and later, for an objective evaluation, an elastography was used.
Later on, the onset of muscle mass loss was assessed by the pitting angle, which is created at the midrange muscle at the contraction stage.
The elastography strain gives an evaluation of the quantitative / semiquantitative damage while shearwave gives us a quantitative evaluation of the damage
With the new AMFT ultrasound technique, ultrasound scans are performed at epigastric levels, taking the upper mesenteric artery vases into abdominal aorta conseration.

### Results

In patients, prior to treatment, the dermis was analyzed ultrasonically.
Several areas emerged: the most superficial color in the dark given by the spacer, a hyperechogenic line consisting of the epidermis, the SLEB dermapapillary line, and finally a hyperechogenic area of the reticular dermis.
In particular, the SLEB's hyperecogenic line was homogeneous at zero stage according to the quantitative classification of the dermis.

After the treatment a dermatitis was performed and a significant recovery of the hyper-structure of the structure was observed. This was also confirmed by elastoecography, as before the treatment the SLEB line appeared blue and therefore showed a rigidity of the structure, after treatment the SLEB line was no longer appreciated.

**Conclusions**

The diagnostic method used, ultrasound, has an important objective value in relation to the ability to make immediate diagnoses and to avoid the use of reactive substances that can be harmful to the patient. It is a non-invasive, reliable and low-cost technique that allows you to evaluate response to therapy and determine the degree of disease in real time.

As far as the new AMFT technique is concerned, this site was chosen as the fat tissue was well represented and measured, and it was not affected by overflapping of organs and by eventual distension of loops of bowel.

The ultrasonographic AMFT evaluation is strongly correlated to the presence of metabolic syndrome and could be a valuable tool for predicting metabolic diseases and associated cardiovascular risks in men.

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## 10. Role of Minerals in Ketogenic Diets

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### Background

The ketogenic diet consists of an almost exclusive protein intake with an high-fats and restrected carbohydrates percentage, that force the body into a ketosis state so that use their own energy reserves and rapidly reduce fat mass. During ketogenic diet it is essential increase the intake of alkaline substances to compensate metabolic acidosis and the loss of mineral salts.

### Hypothesis/Purpose

The weight loss in this hyperprotectic diet is due to the loss of water (caused by the decrease in calories) and the decline in appetite induced by ketosis (it causes acidic radicals that can damage tissues, especially the kidneys). When the body is in carbohydrate deficiency, it doesn't use energy-saving fats and glycogen reserve, but it uses proteins that is introduced with food and partly also muscle protein, and their deamination results in aminoacids (leucine, isoleucine, valine, glutamic acid, aspartic acid, alanine, cysteine, glycine, proline, serine and threonine) needed to synthesize glucose and used for energy purposes. These metabolic processes produce many scavengers such as uric acid and other acids that, to avoid depositing at the articular level, are eliminated together with calcium and water through the urine. When the organism does not intake enough calcium with the diet, the acids released during metabolism will affect bone calcium, causing osteoporosis and kidney stones.

### Study Design

The ketogenic diet is associated with a number of side effects. The classic ketogenic diet is poor in minerals and vitamins, and needs to be supplemented with supplementations to prevent known deficiencies. Some side effects are potentially treatable, such as dehydration but most patients have a mild acidosis at baseline. Effects of the diet, especially hypocitruria, hypercalciuria, and aciduria, can contribute to stone formation (most commonly consisting of urate or calcium). Kidney stones are an adverse event of the ketogenic diet, which occurs in approximately 6% of the children who are started on this treatment for intractable epilepsy. Potassium citrate is a daily oral supplement that alkalinizes the urine and solubilizes urine calcium, theoretically reducing the risk for kidney stones. Moreover, inadequate calcium intake and limited sun exposure can impair bone mineralization, especially in children already at risk of osteopenia and osteoporosis due to long-termant epileptic drugs therapy. Despite bone-sparing effects of improved vitamin D status, some data indicate that use of the ketogenic diet treatment may lead to growth failure, alteration in body composition, and osteopenia in some patients.

### Methods

A cohort study was performed of children started on the ketogenic diet for intractable epilepsy (n = 195). Children who developed kidney stones were compared with those without in terms of demographics, urine laboratory markers, and intervention with urine alkalinization (potassium citrate).Thirteen children (6.7%) developed kidney stones. The use of oral potassium citrate significantly decreased the prevalence of stones and increased the mean time on the ketogenic diet before a stone was first noted. The prevalence of kidney stones did not correlate with younger age or use of carbonic

anhydrate inhibitors (topiramate or zonisamide) but trended toward higher correlation with the presence of hypercalciuria.

**Results**

No child stopped the diet due to stones. Kidney stones continue to occur in approximately in 20 children on the ketogenic diet, and no statistically significant risk factors were identified. Oral potassium citrate is an effective preventive supplement against kidney stones in children who receive the ketogenic diet, achieving its goal of urine alkalination.

**Conclusion**

The micronutrient content of the diet needs to be examined for the restriction of two major food groups; it is not enough to increase the intake of vegetables, as it is rich in both mineral salts and vitamins, indeed intaking vegetables excessively increases the risk of malabsorption or partial absorption of nutrients as iron, calcium and vitamins.

The beneficial supplements for ketogenic diet are those that guarantee the coverage of water and vitamin requirements. It is desirable to give preference to salts containing alkalis, such as citrates (potassium citrate, magnesium citrate, sodium citrate) or bicarbonates (sodium bicarbonate, potassium bicarbonate, etc.).

Calcium, vitamin D, phosphorus, and magnesium are required for bone mineralization, therefore long-term therapy can impair vitamin D metabolism which regulates calcium and phosphorus homeostasis, and thus bone formation and maintenance. The supplementation of calcium and vitamin D sometimes fails to prevent the progress of osteoporotic change, but might improve this condition
to prevent the progress of osteopenia during the ketogenic diet.

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## 11. Ketogenic diet and Epilepsy

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### Background

Mitochondrial disorders are a clinically heterogeneous group of disorders that are caused by defects in the respiratory chain, the metabolic pathway of the adenosine tri-phosphate (ATP) production system. Epilepsy is a common and important feature of these disorders and itsmanagement can be challenging. Epileptic seizures in the context of mitochondrial disease areusually treated with conventional anti-epileptic medication, apart from valproic acid. However,in accordance with the treatment of intractable epilepsy where there are limited treatment options, the ketogenic diet (KD) has been considered as an alternative therapy.

### Purpose

The KD is currently being used therapeutically for intractable epilepsy and for rare diseases of glucose metabolism, where it is the preferred first-line treatment. There is growing evidence to suggest that the KD should also be considered early in the treatment of other epilepsy syndromes like Dravet, West syndrome and myoclonic-astatic epilepsy (Doose syndrome);( Cross, J.H et al, 2010; Baranano, K.W et al, 2008).

### Methods

The use of the KD has been proven to be a safe and effective treatment in intractable epilepsy in numerous studies. The diet was popular for the treatment of epilepsy during the 1920s and 1930s, but drugs were easier to give to patients than trying to put them on a diet that needed careful limitation and management. The diet began to regain publicity again from 1995 due to Jim Abrahams (Hollywood producer) and his son Charlie. Charlie had refractory epilepsy after having tried multiple drugs and surgery; when put on the KD his seizures stopped completely.

Then Freeman et al. (1998) conducted a prospective study of 150 children aged 1-16 with retractable seizures. The age range used as it is proposed that younger children are more responsive but there is only a marginal difference in age range here. Part of the success comes in being able to have no medication as it shows the KD is effective in its own right in management of seizures. Further evidence of the KD decreasing seizure frequency was shown in a prospective study of 65 children aged 18 months to 14 years 6 months (Pulsifer et al., 2001). After one year the mean seizure frequency had decreased from 25 (baseline before treatment) to less than two per day. This is an 88% decrease in mean reduction of seizures.

A few years later Jarrett et al. (2008) demonstrated that the KD confers protection to the mitochondrial genome against oxidative insults, increasing the levels and stimulating de novo biosynthesis of mitochondrial glutathione and improving mitochondrial redox status. This results in improved cellular metabolism and may explain the KD's efficacy in mitochondrial diseases.

Zhu et al. (2016) compared their data obtained by treating 42 children with the classic KD, for intractable epilepsy, with those before the KD treatment and found statistically significant differences. It was concluded that the improvement in neurobehavioral outcome was dependent on clinical seizure control and the benefit was more pronounced with prolonged length of treatment with the KD.

## Results

Most likely, this will not alleviate all forms of epilepsy nor the potential biological pathways causing the seizures, such as glucose/amino acid transport, mitochondrial dysfunction, or neuronal myelination. Considering our current inability to test every individual effectively for the true causes of their epilepsy and the alarming number of misdiagnoses observed, we propose the use of the ketogenic diet (KD) as an effective and efficient preliminary/long-term treatment. The KD mimics fasting by altering substrate metabolism from carbohydrates to fatty acids and ketone bodies (KBs). Here, we underscore the need to understand the underlying cellular mechanisms governing the KD's modulation of various forms of epilepsy and how a diverse array of metabolites including soluble fibers, specific fatty acids, and functional amino acids (e.g., leucine, D-serine, glycine, arginine metabolites, and N-acetyl-cysteine) may potentially enhance the KD's ability to treat and reverse, not mask, these neurological disorders that lead to epilepsy.

## Conclusions

There is growing evidence of the benefits of the KD and its variants in the treatment of a variety of neurological and neurodegenerative disorders. This suggests a possible common central mechanism that improves cellular metabolism and allows cells to resist metabolic challenges that lead to apoptosis.The epigenetic mechanism of action of the KD means it can alter the course of the epilepsy (Schaefer, A.M et al,2008), and may explain why its anticonvulsant effects are long-lasting, even after the KD is stopped.

The safety of the diet also needs to be investigated further in the younger population as the randomized controlled study by Neal et al. only looked at children older than 2 years [ Neal, E.G. et al 2008,]. More work needs to be done to establish which patients would benefit the most, especially when the diet is being considered for a wider range of neurological disorders.

Although there is a significant body of evidence that supports the use of the KD in intractable epilepsy, more studies need to be done looking specifically at its effect in intractable epilepsy in the context of mitochondrial disorders.

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## 12. Comparisonof pea protein and milk protein in treatment for overweight and obesity

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### Background

Overweight and obesity have become a major health problem and strategies for prevention and treatment are needed. The most effective treatment is to decrease food intake, thereby modulating appetite sensations. Among themacronutrients, it seems that protein has the highest satiating effect when compared to other macronutrients in humans and animal studies,helping patient's compliance to dietary recommendations.

### Hypothesis/Purpose

For the importance that may have feeling satiety during a dietwe want totake into consideration the usefull to introduce the pea protein instead of the whey protein in dietary treatments in order to match the interest evenof those increasing patients which present digestive and gastrointestinal disturbs related to any protein derived from milk or which refuse the treatment due to ethical reasons.

### Study Design

So far have been compared the animal protein's integration (as the whey protein that will be considered) and the vegetable protein's integration (as the pea protein that will be considered) for their biological value which is in favor of the former. We actually consider fundamental comparing even the biodisponibility, termogenicity and, moreovertheir level of digestibility and satiety induction. In particular in this studywe want to analyze thesatiation which results from signals that are produced in the gut in response to food-induced mechanical and chemical stimuli, such as the release of the satiety hormones cholecystokinin (CCK), glucagon-like peptide 1 (GLP-1), peptide YY (PYY) and Ghrelin (Ghr)

### Methods

The first technique that was used was the *in vitro* cell culture system. The STC-1 cell line, derived from an intestinal tumor arising in double transgenic mice, is known to secrete CCK and GLP-1 after exposure to nutritional compounds. STC- 1 cells were incubated with several different proteins, hydrolysates, and synthetic peptides, and CCK and GLP-1 release was measured.
The second technique was *in vivo*: overweyght and obese subjects randomly received either pea protein solutions or whey protein solutions, either orally or intraduodenally via a nasoduodenal tube. Appetite-profile, plasma Ghr, GLP-1, CCK, and PYY concentrations were determined over a 2h period. After 2h, subjects received an ad libitum meal and food-intake was recorded.

### Results

There was modest evidence with respect to satiety by pea proteins. Different exogenous biopeptides produced differences in release of endogenous peptides that had inconsistent relationships with satiety. Therefore, evidence derived from a supposed biomarker for satiety does not guarantee the highest satiety.
Some indications of lower hunger, desire to eat and thirst were shown after consumption of pea protein hydrolysate compared to whey protein.A longer intermeal interval and a higher satiety index were suggested after consumption of pea proteins.

**Conclusions**

Even thougha particoulargastroprotection by alpha-lactalbumin has been demostrated, pea protein is to be considered as a sustainable, satiety-inducing food ingredient to take in accountin treatment for overweight and obesityin those kinds of patients which have digestive problems.

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## 13. Hazelnut (*Corylus avellana* L.) by-products: from wastes to resource of chemopreventive and anti-*Candida albicans* polyphenols

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### Background

Hazelnut (*Corylus avellana* L., Betulaceae) is one of the most popular edible nuts used as whole fruit (raw or roasted) and as an ingredient in processed foods. A huge amount of by-products, namely shells and skins, are obtained from the kernel industrial processing.

### Hypothesis/Purpose

The disposal regarding this biodegradable waste material represents an environmental and economic problem for the hazelnut-industry, and its recovery and recycling may be of a great interest. In recent years, attention has been paid to the hazelnut wastes as sources of bioactive compounds with beneficial effects on human health.[1]

### Results

The present research aimed to study polar extracts from the shells (HSE) and skins (RHS), kindly supplied by a food industry. The analytical investigation led to the isolation and NMR characterization of neolignans, phenolic compounds, and a diarylheptanoid from HSE. Among them the major constituents were quantified (HPLC-DAD method). RHS appeared rich in oligomeric proanthocyanidins (PAs) mainly constituted by B-type oligomers of (epi)-catechin. Also A-type PAs were detected and (epi)-gallocatechin and its gallate derivatives was identified as monomer units by UHPLC-UV, FIA-HRMS and UHPLC-MS/MS techniques. HSE exhibited a concentration-dependent inhibitory effect on melanoma cancer and cervical carcinoma cell growth showing a pro-apoptotic effect. The activity relies on the presence of neolignans and gallic acid. RHS was effective against *Candida albicans* SC5314, due to its PAs-rich fraction, as determined by the micro-broth dilution method and Candida morphological analysis.[2,3]

### Conclusion

Our results showed that hazelnut wastes can be considered as newsworthy sources of bioactive compounds with promising chemopreventive and antifungal properties.

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## 14. Effects of Ketogenic Diet on Insulin Levels: Treatment of Insulin-Resistant Pathologies

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### Background

Ketogenic diets are characterized by reduced carbohydrate intake in the diet that can induce a state of physiological ketosis. Such diets can correct insulin resistance, a condition that predisposes to a variety of diseases that are increasingly common among westerners. There are several evidence of the metabolic benefits of ketogenic diets : from obesity therapy to type 2 diabetes (T2DM), to polycystic ovary syndrome (PCOS) or non-alcoholic liver steatosis.

### Hypothesis/Purpose

The purpose of this review is to analyze the literature on the direct effect of physiological ketosis on insulin levels, and to re-evaluate the dietary treatment of all pathological conditions associated with insulin resistance in favor of the ketogenic diet.

### Study Design

Article, Review

### Methods

A pubmed research was conducted using keywords such as "ketogenic diet" and "insulin resistance".

### Results

Both insulin and ketones have the same effects on the metabolites of the first third to the citric acid cycle, on mitochondrial redox states and both increase the hydraulic efficiency of the working perfused heart. Viewed in this light, mild ketosis provides the same metabolic effects as insulin, but at the metabolic or primitive control level which by-passes the complex signaling pathway of insulin. During prolonged fasting, when insulin levels approach 0, mild ketosis compensates metabolically for the absence of insulin effects. It follows that the induction of mild ketosis would be therapeutic in insulin resistant states[1]. Insulin resistant states are extremely common. Insulin resistance and hyperinsulinaemia appear to be linked to PCOS, independently of obesity, and modifications in the normal cellular mechanisms of insulin signalling have been demonstrated in both lean and obese patients [2]. A pilot study showed that adherence to a low-carbohydrate, ketogenic diet led to improvement in body weight, percent free testosterone, LH/FSH ratio, fasting serum insulin, and symptoms in women diagnosed with PCOS over a six-month period[3]. The hyperinsulinemia of PCOS appears to increase androgen secretion from the ovary as well as to decrease circulating sex hormone binding globulin (SHBG) [4]. The study suggested that a LCKD (low carbohydrate ketogenic diet) may lead to a reversal of these processes. We speculate that reduction in hyperinsulinemia due to the LCKD would decrease stimulation of ovarian androgen production as well as increase SHBG levels, synergistically limiting the amounts of circulating free-androgens in the serum. In addition, the reduction in LH/FSH ratio exhibited in this study may be indicative of endocrine re- normalization resulting from the LCKD intervention, due to an improvement in insulin sensitivity.

Insulin resistance is the hallmark of type II diabetes and the socalled "metabolic syndrome" where it is associated with visceral obesity and hypertension [5].

Hussain et al. [6] compared a VLCKD (very low calorie ketogenic diet) with a low-calorie diet (LC) over a 24 weeks period in 102 diabetic and 261 nondiabetic individuals. In VLCKD diabetic group fasting blood glucose decreased in normal range, but this did not occur in LC diabetic group, whose blood glucose concentration leveled out at 16 wk and remained elevated. At 24 wk average $HbA_{1c}$ in VLCKD diabetic group is 6,2%, whereas in LC diabetic group it remained >7,5%. In healthy controls, none of the diets produced significant changes in fasting blood glucose, that was already at normal level, and $HbA_{1c}$.

In a similar study Goday et al. [7], compared efficacy of a VLCKD versus hypocaloric diet (based on American Diabetes Association guidelines) in 89 patients with T2DM, over a 4 months period. At the end of the study in VLCKD group average fasting blood glucose is 198,9 mg/dL (baseline 136,9 mg/dL9, whereas in other group is 123,3 mg/dL (baseline 140,5 mg/dL); in VLCKD group average $HbA_{1c}$ is 6% (baseline 6,9%), whereas in other group is 6,4% (baseline 6,8%); in VLCKD group HOMA-IR index dropped to 3,5 from initial value of 6,9, whereas in other group it decrease from 5,8 (baseline) to 4,6. In the VLCKD group, 33 subjects were treated with oral antidiabetics, but at 16 wk only 20 continued using these medications, while in the other group from 38 patients using oral antidiabetics, to 30 using these drugs.

Another study by Westman et al. [8], compared the effect on glycemic control of a LCKD (without calorie-resticition) versus low-glycemic index reduced-calorie diet (LGID), in 97 patients (49 completed the study) over a 24 wk period. At 24 wk in LCKD group fasting blood glucose has decreased on average -19,9 mg/dL, versus -16 mg/dL in LGID group; fasting insulin has decreased on average of -6 uU/mL in LCKD group, while only -2,2 uU in LGID group; in LCKD group $HbA_{1c}$ has decreased on average -1,5%, whereas in LGID group -0,5%.

## Conclusion

Data reported in literature confirm the greater efficacy of ketogenic diet than other dietary therapies in the treatment of pathologies related to insulin resistance.

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## 15. The risk of hypokalaemia induced by a ketogenic diet associated with pharmacological treatment with thiazide-diuretics

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### Background

The ketogenic diet may induce the risk of hypokalaemia(1). If the diet is associated with a thiazide or diuretic drug therapy, you may have an exacerbation of this side effect.

### Hypothesis/Purpose

The purpose of this study is to analyze the risks associated with the administration of thiazide diuretic drugs in patients following the ketogenic diet. It is supposed that the combination of thiazide diuretics with the ketogenic diet causes various side effects, including hypokalaemia(2).

### Methods

A study was carried out to compare patients following the ketogenic diet in combination with thiazide diuretic drugs and patients following the ketogenic diet in the absence of drugs. As a result, the risk of hypokalaemia was measured. The protocol consists of a pre-visit that involves the execution of analytical tools such as ECG at rest and under stress. The presence of an abnormal "U" wave in the ECG trace indicates hypocalemic changes and consequent cardiopathy(3). Subsequently, laboratory tests are performed that consist of blood sampling and therefore analysis of certain hematochemical parameters such as total cholesterol, HDL cholesterol, triglycerides, glycemia / HbA1c, azotemia, creatinine, uric acid, transaminase, gammaGT, CPK, sideremia / ferritin, hemocromo with formula, complete urine examination. Then, a clinical / anthropometric evaluation is performed: height, weight, waist, hips, pliers, arms circumference; and finally a bio-functional analysis: muscle strength (strength), oxygen consumption, metabolic evaluation (basal and under stress), body composition (bioimpedensometry).

### Results

It has been oserved that patients who followed the ketogenic diet in the absence of diuretic drugs had several side effects but hypocalemia was mild or absent. In contrast, in patients trated with ketogenic diet associated with thiazide diuretic drugs, hypokalaemia appeared to be marked with subsequent side effects such as cardiac disease.

### Conclusion

The ketogenic diet is considered one of the best therapies in the treatment of obesity well as in some diseases such as epilepsy(4,5). Nevertheless, patients following a ketogenic diet should be monitored continuously for side effects. In the event that the patient associates thiazide diuretics with the diet and has low levels of potassium cannot survive or replace such drugs, the diet should be reviewed or suspended(6).

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## 16. Modulation of Human Intestinal Microbiota following a Ketogenic Diet

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### Background

Each year, numerous works is released out on human intestinal Microbiota, demonstrating the great interest and the great importance of this "organ", which has many functions within our body. Microbiota's science has flourished in recent years and the stimulating discoveries resulting from this increase in interest have forced us to re-evaluate our perception of the vast amount of microorganisms present in the human gastrointestinal tract whose composition is specific to each individual. Although we are just beginning to understand the concept of Microbiota, we already know that its composition has a profound impact on human health. A key factor for the determination of intestinal Microbiota is diet, which also results in changes in the composition and diversification of the bacterial species that compose it. Preliminary evidence suggests that possible dietary models are associated with distinct combinations of bacteria in the intestine and currently know food constituents that promote the growth of beneficial bacteria in the intestine. In fact, the diet can have a strong impact on the intestinal environment, especially the intake of the three major macronutrients (carbohydrates, proteins and fats) that can significantly affect the composition of the Microbiota. Western diets, as well as particular dietary approaches such as ketogenic diet, can result in a significant modification in the composition of the Microbiota.

### Hypothesis/Purpose:

In this abstract we report the changes that human intestinal Microbiota undergoes following various food regimens(Mediterranean, Oriental, African, Nordic, Vegetarian, Ketogenic, Gluten-Free and Caloric Restriction) and changes made by individual nutrients, focusing mainly on the actions of proteins and ketone bodies produced in a ketogenic diet regime, as well as evaluating possible useful outcomes in order to restore an altered intestinal Microbiota.

### Study Design

Narrative review with experimental animal model studies and population studies on humans.

### Methods

The abundance and diversification of the Microbiota components can be analyzed through various techniques ranging from the most common collection and culture of faecal samples to more modern and efficient methods such as Fingerprinting, Dot-Blot hybridization or in situ fluorescence hybridization. DNA sequencing has created genes database and the one most used for Microbiota

analysis is the rRNA 16S gene. Among the new methods we have the combined use of stable isotopes and biomarkers useful in studying the metabolic activities of individual groups or organisms in situ.

**Results**

Numerous evidences have shown that different diet plans can significantly influence the composition of the intestinal Microbiota resulting in the proliferation of certain microbial strains and reduction of others. In the case of ketogenic diets there are microorganisms that do not undergo modifications while others are very sensitive to proteins or ketone bodies. Specifically, ketogenic diets cause a reduction in *Lactobacillus*, *Prevotella*, *Bacteroides* and *Enterobacteriaceae*.

**Conclusion**

Current knowledge about intestinal microbiosis shows that it is not a "silent organ" or simply a collection of host microorganisms but microbial communities are active actors in a complex organic mechanism. Numerous emerging studies can help the scientific community better understand this complex "forgotten organ". Compelling evidence, as demonstrated, supports the importance of the microbial community along with proper dietary styles but many efforts still need to be devoted to the study of the properties that characterize individual species and bacterial strains, also with reference to the phenotypic and genetic subtypes of patient and different pathologies. The development of effective analytical methods will lead to an increasing understanding of the complexity of intestinal microbiosis and this will lead to new questions about the mechanisms through which intestinal bacteria interact with humans. This will also allow the development of future treatments, in synergy with ketogenic protocols, for increasingly emerging gastrointestinal diseas.

## 17. The Use of Probiotics and Prebiotics to Prevent Gastrointestinal Complications During Ketogenic Diets

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**Background**

According to the official definition of FAO and WHO, "probiotics"are "living organisms that, given in an adequate amount, make a benefit to the hospital's health". This definition refers to non-pathogenic microorganisms present in foods or added to them, and "excludes references to bioterapeutic agents and beneficial micro-organisms not used in food".

While, it is defined as prebiotic, not to be confused with the probiotic, any substance that is present in the food is not absorbed by the organism but is used by the intestinal flora. Prebiotics were identified and named in 1993 by Marcel Roberfroid. In the vast majority, carbohydrates, in particular oligosaccharides. Prebiotics promote the growth and activity of Bifidobacterium and Lactobacteria, bacterial species important to the digestive health of the host organism.

**Hypothesis/Purpose**

The approach of modulating the gut flora for improvedhealthhasmuchrelevance for the management of those with acute and chronicgutdisorders.

Probioticingestion can be recommendedas a preventiveapproach to maintaining the balance of the intestinal microflora and therebyenhance 'well-being'.

The probioticapproachhasbeenextensivelyused and advocated, survivability/viabilityafteringestionisdifficult to guarantee and almostimpossible to prove.

**Methods**

The prebioticconceptdictatesthat non viabledietarycomponentsfortifycertaincomponents of the intestinal flora (e.g., bifidobacteria, lactobacilli). Thisconceptthas the advantagethatsurvival of the ingestedingredientthrough the uppergastrointestinaltractis not a prerequisitebecauseitisindigenousbacterial genera that are targeted. The feeding of oligofructose and inulin to human volunteersalters the gut flora composition in favor of bifidobacteria, a purportedlybeneficialgenus. In Ketogenicdiet, increasing the dose of inulin and oligofructose, itimproves the condition of intestinalbacteria in the patient under the use of Ketogenicdiet.

Onepossiblemechanism for the action of probioticsistheirability to adhere to the intestinal mucosa.

**Results**

Probioticswillvary in theirefficacy and itmaynot be the case that the sameresultsoccur with allspecies. Thosethat prove mostefficientwilllikely be strainsthat are robustenough to survive the harshphysico-chemicalconditionspresent in the gastrointestinaltract. Thisincludesgastric acid, bile secretions and competition with the resident microflora. In theory, increasedlevels of probioticsmay induce a 'barrier' influenceagainst common pathogens.

**Conclusion**

The approach of modulating the gut flora for improvedhealthhasmuchrelevance for the management of those with acute and chronicgutdisorders.

The directeffects of a change in dietarypatterns and eatinghabits can affectoverallgutfunctionality.

Itis of considerable benefit to the host, therefore, to maintain a good community structure, throughincreasedlevels of bacteriasuchas lactobacilli and bifidobacteria, preferablyat the expense of more harmfulorganisms.

## 18. Ketogenic diet and its role in visceral fat reduction

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### Background

Visceral fat mass is closely correlated with obesity-associated pathology. In particular, truncal adiposity is strongly associated with the insulin resistant metabolic syndrome.

### Hypothesis/ Purpose

Visceral adipose tissue is not simply a story of excess energy, but a secretary organ, releasing a wide range of protein factors and signals, named adipokines, in addition to fatty acids and other lipid molecules.The circulating levels of inflammatory factors, such as TNF-alfa, IL-1, IL-6, IL-8, IL-10, chemiotactic proteins, vascular endothelial growth factor, increase along with intraabdominal fat accumulation. Many of these factors are produced by visceral adipocytes and by resident macrophages, which are recruited by circulating monocytes through chemotactic factors produced by hypertrophic adipocytes. This low-grade chronic inflammation leads to a progressive deterioration of glucose tolerance, that can be prevented only if the ß-cell is able to increase its insulin secretary response, maintaining a state of chronic hyperinsulinemia. A low-carbohydrate ketogenic diet is associated to a drastic reduction of insulin, the most important lipogenic hormone in the adipose tissue. It involves visceral fat mass loss, increasing metabolic rate and improved glycemic control.

### Study design

Patients follow a two-stage weight loss program: 3 weeks of ketogenic diet (Oloproteic Diet [OD]) followed by 6 weeks of low glycemic hypocaloric (hypo-MD) diet.

### Methods

During the Oloproteic Diet phase, patients were on a very low calories diet (<500 kcal/day) based on protein, providing about 10-20 g of carbohydrate and lipid per day. The sources of these macronutrients are vegetables, olive oil, and protein-rich foods. The total daily protein content of the Oloproteic Diet was set at 1.4 g per kilogram of ideal body weight. Half of this protein intake was provided by administering a liquid formulation containing a fixed portion (1: 6.5) of essential aminoacidis (arginine, ornithine, alpha-keto-glutarate, taurine, cysteine, tryptophan, hydroxyproline and citrulline) and proteins of high biological value like those of whey proteins. This phase has been completed by the daily administration of alkalinizing substances, to contrast ketosis effect: calcium carbonate, 1500 mg daily; magnesium carbonate, 850 mg per day; potassium bicarbonate, 500 mg per day; sodium bicarbonate, 1500 mg daily; potassium citrate, 500 mg daily, herbal products generally prescribed for their diuretic, antioxidant, anti-inflammatory and hepato-protective properties containing equiseto, hawthorn, cardo mariano, orthosiphon and fucoxanthin; and a complete multivitamin and multimineral supplement. Patients had to drink water or beverages (no tea or coffee) without sugar, recommending a minimum dose of 2 L/day. In patients with a history of kidney stones, the amount was increased to 3 L. To avoid unintentional hypoglycemia and electrolyte imbalance, all treatments with hypoglycemic and diuretic drugs were suspended before starting treatment. Antihypertensive and uric acid drugs and hypolipidemic drugs have not been changed.

During Phase II, patients were on a low-calories diet that provides 25-30 kcal / kg body weight per day (54% carbohydrates, 18% protein energy, and 28% fat [saturated ,<7% in line with Mediterranean Diet

standards). Patients added more vegetables and consumed no more than two portions of fruit per day in order to increase the intake of fibers up to 30-35 g per day without exceeding the sugar intake. Finally, olive oil was the main source of fat, while alcohol was not allowed. Additionally, patients continued to take herbal remedies, as well as amino acids and whey proteins (only for breakfast, a 15 g sachet) for maintaining muscle mass during weight loss.

**Results**

Data on the following parameters were collected at day 0 and at the end of both phases (day 22 and day 64 respectively) before any pharmacological treatment was reintroduced. Constipation and muscle spasms were the most frequently reported side effects (during OD, 19.2% and 17.8%, respectively).However, their frequencies were significantly reduced during the second phase of the study (11.0% and 2.7%, respectively).Other less frequent side effects (< 5%) reported only during the first phase of surgery, were headaches and palpitations.Weight loss was elevated in both phases of intervention: 7.5% and 10% of the initial body weight, respectively in 100% and 87.7% of patients. Biochemical parameters have also confirmed the substantial safety of the proposed intervention. In particular, no alteration (value outside the normal laboratory interval) occurred in major serum electrolytes, hepatic enzymes and renal function parameters, although a light increase in uric acid was observed at the level During the OD phase.

The OD phase was associated with a significant improvement in visceral adiposity,measured through the evaluation of aort-mesenteric fat,in GH levels ,a lipolytic hormone,andin metabolic parameters, particularly those related to glucose and lipid metabolism; although an expected drop in HDL cholesterol has been reported.OD was responsible for a significant decrease in the IGF-1 (insulin-like growth factor). Besides, it is associated with increased sympathetic stimulation which is a key determinant of lipolysis within visceral fat. All these factors contribute to the disruption of the vicious cycle sustaining the insulin-resistance dyslipidemic syndrome and the related cardiometabolic complications. A complete return to baseline levels of IGF-1 was observed at the end of the ipo-MD phase, during which a reduction in GH was also observed (however, GH levels were higher than those for starting study). The ipo-MD phase was also responsible for a persistent positive effect on visceral adiposity and liver function enzymes, and for a significant reduction in uric acid values.

**Conclusions**

A ketogenic diet, in addition to the weight loss, offers the patient:a global glycometabolic control in most of patients with a drastic reduction in drugs and consequent reduction in pharmaceutical spending, improved quality of life and increased pharmacological productivity; a lasting reduction in cardiovascular risk; a reduction in the risk of oncologic IGF-1 dipendent disease.

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## 19. Trans-Differentiation of Adipose Tissue: Clinical Implications

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### Background

The adipose organ represents a special loose connective tissue containing adipocytes and several cell types surrounded by capillary and innervation networks (i).White adipocytes are primarily involved in storing energy while brown ones substantially dissipate energy to maintain body temperature in cold environments. Although it was thought that the brown adipocytes exist only in infants humans, it has been demonstrated that they can be present also in the adults. A trans-differentiation theory has been proposed. In the last years, there has been growing interest in the characterization of adipose tissue, particularly its functions and how these could change and be influenced by exogenous and endogenous factors.

### Hypothesis/Purpose

We narratively reviewed the available evidence on exogenous and endogenous responsible for the trans-differentiation of adipose tissue, particularly the browning of white adipocytes.

### Methods

Relevant English-language articles were searched through electronic databases (PubMed and Medline).

### Results

Retrieved articles were primarily focused on the role of adrenergic nerve stimulation (and its connection with lipolysis and lipid oxidation), hormones, thermogenesis-induced gene expression, low temperature as well as emerging nutritional factors. Although in theory, an increase in physical activity could provide the solution to treat and prevent obesity, in practice, the compliance in sustaining regular exercise is also poor, and there is increased recognition of the need for alternative or complementary strategies to enhance energy expenditure. Chronic cold exposure transforms white adipocytes into brown ones to supply the thermogenic needs, and conversely, brown adipocytes transform into white adipocytes when the energy balance is positive and the adipose organ requires increased storage capacity (ii). However, the browning seems to be primarily mediated by the sympathetic nervous system through the beta3-adrenoreceptor (β3-AR) (iii). Therefore, sensitizers or activators of the associated intracellular transduction pathway could also be considered as useful therapeutic agents in obese patients. However, trials with β3-AR agonists were unsuccessful (iv). On the other hand, patients with pheochromocytoma were found to be characterized by substantial white-to-brown trans-differentiation (v). These data suggest that white-to-brown transdifferentiation

also occurs in humans and might be harnessed for therapeutic purposes. A range of new molecular mechanisms to induce browning have recently been proposed. Among these, secreted factors such as ANP (NPPA), BMP8B, irisin and FGF21 that affect brown adipocyte activation and recruitment are of increasing interest (vi).
However, the plasticity is not limited to browning phenomenon because during pregnancy, lactation or postlactation states in females, white adipocytes in mammary glands seem to have the ability to convert into milk-secreting epithelial cells (vii). Each function is critical for individual and species survival.

**Conclusion**

The knowledge of signaling pathways associated with factors involved in adipose tissue trans-differentiation represents an opportunity for identifying new strategies for the management of obesity-related complications. However, knowledge has been mainly collected in animal-model studies and findings cannot be fully extrapolated to humans. The same factors deserve further investigation.

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## 20. Hungry cells

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### Background
Healthy lifestyle and a balanced diet with a variety of ingredients and other substances may help blocking diseases like cancer at early stages.

### Hypothesis/Purpose
Is it possible for foods to help fighting a disease like cancer?
Some substances are able to slow the growth of tumor cells; others facilitate apoptosis, the "programmed suicide" of cells, a natural body-protective mechanism that tumor cells know how to escape.Others do have anti-angiogenetic properties, by blocking the development of new blood vessels close to the tumors, making them difficult to nourish and thus enlarge.
Finally, a high number of food elements can act on the so-called micro-environment, or on the general state of the body near the cells, thus facilitating the work of the immune system and hindering tumor cells, preventing them from creating an environment that facilitates their growth.
For example, the successful treatment of malignant gliomas remains a challenge despite the currentstandard of care, which consists of surgery, radiation and temozolomide. Advances in thesurvival of brain cancer patients require the design of new therapeutic approaches that takeadvantage of common phenotypes such as the altered metabolism found in cancer cells. Ithas therefore been postulated that the high-fat, low-carbohydrate, adequate protein ketogenicdiet (KD) may be useful in the treatment of brain tumors. Actually,the KD enhances survival and potentiates standard therapy in a mouse model of malignantglioma, yet the mechanisms are not fully understood(10).

### Study Design
literature review.

### Methods
Articles published in scientific journals have been assessed regarding the impact of a ketogenic dietary regimen on the disease progression. Please see the references section for further details.

### Results
Almost all cancer (5, 8)cells share a common trait: they use carbohydrates and / or glucose in the blood to grow and multiply.With time and growth, cancer cells become more and more glucose-dependent; a proper ketogenic regimen alters some of the standard metabolic processes, lowers glycemic blood levels and, in fact, afflicts tumor cells.
The long-term effects of this limitation can lead tumor cells to grow more slowly, diminish in size, or even die. A ketogenic diet is feasible and likely beneficial for patients with cancer in primary care, who have been treated for their primary cancer, since it altered the expression of TKTL1, a novel and potentially useful marker to monitor the metabolic state of the body regarding aerobic glycolysis, and to evaluate the potential progression of non endstage tumor disease(6).

Many decades ago, Otto Warburg suggested that cancer cells exhibit an increased capacityto utilize glucose and produce lactate even when an adequate supply of oxygen is present. While incompletely understood, increased glycolysis in tumor cells may be important for productionof non-essential amino acids such as serine. In cancer cells, the majority of pyruvateis converted to lactate and glutamine is utilized for replenishing tricarboxylic acid cycle intermediates. In the brain, cells primarily metabolize glucose but they can switch toketone use under low glucose conditions. The ketone bodies, acetoacetate and D-β-hydroxybutyrate,are produced in the liver via fatty acid oxidation, transported to extrahepatic tissues andtaken up by cells where they enter the tricarboxylic cycle as acetyl-CoA. The brain uses ketonebodies at a rate that is directly proportional to their concentrations in arterial blood. However, little is known about the utilization of ketones in brain tumor cells. Studies, carriedout in mouse models, show that brain tumor growth can be reduced by placing mice on a calorie-restricted, low carbohydrate, high fat diet. Mice bearing malignant astrocytomas and orthotopicallyimplanted human malignant gliomas exhibited reductions of 65% and 35% in tumorburden, respectively when fed a low carbohydrate, high fat diet. Additionally, an orthotopicglioma mouse model showed prolonged survival after radiation treatment when maintainedon a low carbohydrate, high fat diet. These findings led to the proposal that aketone-producing, low glucose diet hinders growth of brain tumor cells because they cannotefficiently use ketones when the supply of glucose is limited (8).

Calories restriction (CR) extends lifespan and has been shown to reduce age-related diseases including cancer,diabetes, and cardiovascular and neurodegenerative diseases in experimental models. Recent translational studieshave tested the potential of CR or CR mimetics as adjuvant therapies to enhance the efficacy of chemotherapy,radiation therapy, and novel immunotherapies. Chronic CR is challenging to employ in cancer patients, andtherefore intermittent fasting, CR mimetic drugs, or alternative diets (such as a ketogenic diet), may be moresuitable. Intermittent fasting has been shown to enhance treatment with both chemotherapy and radiation therapy.CR and fasting elicit different responses in normal and cancer cells, and reduce certain side effects of cytotoxictherapy. Findings from preclinical studies of CR mimetic drugs and other dietary interventions, such as theketogenic diet, are promising for improving the efficacy of anticancer therapies and reducing the side effects ofcytotoxic treatments. Current and future clinical studies will inform on which cancers, and at which stage of thecancer process, CR, fasting, or CR mimetic regimens will prove most effective(2).

Dysregulated energetics coupled with uncontrolledproliferation has become a hallmark of cancer, leading toincreased interest in metabolic therapies. Dietary treatment options basedon glucose deprivation have been explored using a restrictiveketogenic diet (KD), with positive anticancer reports. However,negative side effects and a lack of palatability make the KDdifficult to implement in an adult population. Hence, a less stringent, supplemented high-fat low-carbohydrate(sHFLC) diet that mimics the metabolic and antitumoreffects of the KD, maintains a stable nutritional profile, andpresents an alternative clinical option for diverse patientpopulations(7).

The inability of ketone bodies metabolizing due to various deficiencies in mitochondrial enzymes isthe major metabolic changes discovered in malignant cells. Therefore, administration of a ketogenicdiet (KD) which is based on high in fat and low in carbohydrates might inhibit tumor growth andprovide a rationale for therapeutic strategies. Systematic reviews have been conducted to assess theeffects of KD on the tumor cells growth and survival time in animal studies. Many articles indicate that KD had abeneficial effect on tumor growth and survival time. Tumor types included pancreatic, prostate,gastric, colon, brain, neuroblastoma and lung cancers. In conclusions, although studies in this fieldare rare and inconsistence, recent findings have demonstrated that KD can potentially inhibit themalignant cell growth and increase the survival time. Because of differences physiology betweenanimals and humans, future studies in cancer patients treated with a KD are needed(1).

Malignant brain tumors are devastating despite aggressive treatments such as surgical resection, chemotherapy and radiation therapy. The average life expectancy of patients with newly diagnosed glioblastoma, for example, is approximately _18 months. It is clear that increased survival of brain

tumor patients requires the design of new therapeutic modalities, especially those that enhance currently available treatments and/or limit tumor growth. One novel therapeutic arena is the metabolic dysregulation that results in an increased need for glucose in tumor cells. This phenomenon suggests that a reduction in tumor growth could be achieved by decreasing glucose availability, which can be accomplished through pharmacological means or through the use of a high-fat, low-carbohydrate ketogenic diet (KD). The KD, as the name implies, also provides increased blood ketones to support the energy needs of normal tissues. Preclinical work from a number of laboratories has shown that the KD does indeed reduce tumor growth in vivo. In addition, the KD has been shown to reduce angiogenesis, inflammation, peri-tumoral edema, migration and invasion. Furthermore, this diet can enhance the activity of radiation and chemotherapy in a mouse model of glioma, thus increasing survival. Additional studies in vitro have indicated that increasing ketones such as b-hydroxybutyrate (bHB) in the absence of glucose reduction can also inhibit cell growth and potentiate the effects of chemotherapy and radiation. Thus, while we are only beginning to understand the pluripotent mechanisms through which the KD affects tumor growth and response to conventional therapies, the emerging data provide strong support for the use of a KD in the treatment of malignant gliomas. This has led to a limited number of clinical trials investigating the use of a KD in patients with primary and recurrent glioma (3).
Since the initial observations by Warburg in 1924, it has become clear in recent years that tumor cells require a high level of glucose to proliferate. Therefore, a ketogenic diet that provides the body with energy mainly through fat and proteins, but contains a reduced amount of carbohy¬drates, has become a dietary option for supporting tumor treatment and has exhibited promising results. In a study, 78 patients with tumors were treated within a time window of 10 months. The patients were monitored regarding their levels of transketo¬lase like 1 (TKTL1), a novel tumor marker associated with aerobic glycolysis of tumor cells, and the patients' degree of adherence to a ketogenic diet. Tumor progression was documented according to oncologists' reports. Tumor status was correlated with TKTL1 expression (Kruskal Wallis test, P<0.0001), indicating that more progressed and aggressive tumors may require a higher level of aerobic glycolysis. In palliative patients, a clear trend was observed in patients who adhered strictly to a ketogenic diet, with one patient experiencing a stagnation in tumor progression and others an improvement in their condition. The adoption of a ketogenic diet was also observed to affect the levels of TKTL1 in those patients. In conclusion, the results from the present case series in general practice suggest that it may be beneficial to advise tumor patients to adopt a ketogenic diet, and that those who adhere to it may have positive results from this type of diet. Thus, the use of a ketogenic diet as a complementary treatment to tumor therapy must be further studied in rigorously controlled trials(6).

## Conclusions

The KD may work in part as an immune adjuvant, boosting tumor-reactive immune responses in themicroenvironment by alleviating immune suppression. This evidence suggests that the KD increases tumor-reactiveimmune responses, and may have implications in combinational treatment approaches(4).
The KD directly or indirectly alters the expression of several proteins involved in malignantprogression and may be a useful tool for the treatment of gliomas(12).
Improvements in the survival and quality of life for patients with malignant brain tumors require the implementation of new therapeutic modalities, especially those that increase the efficacy of current therapies without increasing toxic side effects. While the rapid accumulation of data defining the molecular and genetic aberrations present in these tumors has suggested a host of targets for the development of new therapies, targeted therapies tried to date have met with limited success. This is at least in part due to the molecular heterogeneity of these tumors that prevents any one target from being present on all cells. In contrast, metabolic dysregulation is present in virtually all tumor cells and there is increased interest in using metabolic therapies such as the KD and ketone supplementation for

the treatment of various cancers, especially brain tumors. Preclinical data has demonstrated that the anti-tumor effects of the KD and CR are multi-faceted, and alterations in energy metabolism can inhibit cancer cell growth and increase the tumor's response to therapy. This provides a strong impetus to continue work designed to elucidate the mechanisms through which the KD exerts its anticancer effects, as well as suggesting the need for the design of controlled clinical trials that will shed light on the most effective way to implement metabolic therapies in combination with standard therapies for the treatment of malignant disease. This is a novel therapeutic paradigm, and we have only begun to scratch the surface of its potential(3).

Therapies that target the metabolic phenotype of cancer and palliate symptoms or improve quality of life are important in oncologic care and scientific investigation. Over the past decades, clinical trial designs to optimize pharmacologic drug development have been established. These provide mechanisms to document feasibility, safety, and efficacy in early phase studies of new therapeutic approaches. A similarly rigorous approach is required in the investigation, and incorporation of novel strategies aimed at glucose modulation and dietary supplementation for patients with CNS tumors(9).

Consistent with other published studies, we found that serum ketone levels were significantlyincreased and glucose levels only mildly decreased in mice on the ketogenic diet. The ketogenic diet when used in conjunction with radiation has been shown to significantlyreduce regrowth of orthotopic transplanted glioblastoma and flank lung tumors. Thereare only a few cases in which the ketogenic diet has been used in conjunction with drug-basedtherapies in mice (8).

All of the above data and considerations confirm the importance of the KD and CR in the fight of serious diseases like cancer and they do all suggest/recommend further investigations.

Times are changing.Since the year 2002, over 20 human studies have been conducted on low-carb diets.In almost every one of those studies, low-carb diets come out ahead of the diets they are compared to.Not only does low-carb cause more weight loss, it also leads to major improvements in most risk factors... including cholesterol.

Lowering oxidative stress in the body is one way to increase lifespan. It seems that by lowering insulin levels, oxidative stress in turn is decreased. A ketogenic diet decreases insulin levels – allowing the formation of ketones to be used as fuel. Many experts are turning to ketogenic diets in a quest to slow down aging in general. This is another upcoming area of science.

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## 21. Stress, Cortisol, Orexigenic and Anorexigenic Metabolic Hormones as Possible Clinical Targets Related to Weight Gain

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### Background

Stress influences eating behaviour and food choices. Aim of this paper is to investigate this issues in the specific context of contemporary society. Through the study of recent clinical investigation on the hormones role in food craving and weight gain, we will try to highlight the man ypossibilitie sthat the hormones modulation could have in therapy of obesity.

### Hypothesis/Purpose

Energy intake and weight regulation is challenging. American people gain 0,2 to 0,9 kg eachyear and the prevalence of obesity is 37,7% (1).

Among energy and weight regulation mechanisms, stress, cortisol, anorexigenic and orexigenic metabolic hormones have been identified as possible clinical targets.

Stress is a disruption in homeostasis and influences eating behaviors and food choises and the effects depend on the type and duration of them.

Acute stress induces suppression of appetite, otherwise cronic stress promotes wanting, seeking and intake of high fat and energy dense food (2) and has been linked with obesity and weight gain.

The effect of stress on food intake and weight gain can be related to perturbations in the hypothalamic-pituitary-adrenal axis (HPA) that it provides for secretion of cortisol, a glucocorticoid that stimulates appetite and increases food intake. (3)

Other hormones communicate with the central nervous system to signal information about energy homeostasis but their effective role is unclear.

Ghrelin is mainly secreted from the stomach and stimulates appetite and food intake (4) and has been demonstrated that individual with obesity have lower fasting ghrelin levels and attenuated postprandial ghrelin suppression (5), though central and peripheral administration of ghrelin result in weight gain in preclinical models (6).

Insulin and leptin are adiposity signals (7). The beta cells of the pancreas produce insulin to utilize glucose in the body tissues. Leptinis an adipokine made in adipocytes and is involved in satiety signaling.

Leptin and insulin levels are increased in individual with overweight and obesity but the resistence to insuline and leptin possibly, may contribute to dysregulation of hunger and satiety signaling, therefore on the eating behavior.

Has been hypothesized that the effect of cortisol and stress may potentiate the rewarding value of food and increase food cravings, similar to the effects of stress on craving in substance use disorders.

Food cravings are an intense desire of a specific food and it is associeted with great intake of food and increased BMI (8).

The purpose of this study was to examine whether chronic stress, cortisol and appetite related hormones were predictive of future food craving and weight 6 months later.

## Methods

This study reports on 6-month longitudinal changes in weight from a community cohort of 339 participants who completed initial baseline measures and also attended a 6-month follow-up assessment.

Exclusion criteria were pregnancy, dependence on drugs, nicotine, use of prescribed medications for any psychiatric disorders, and serious and chronic medical conditions.

Participants had a morning biochemical evaluation session after fasting overnight, A research nurse or trained research staff member measured participants' weights at baseline and follow-up. These weights and measured heights were used to calculate BMI.

Chronic stress was assessed using the chronic stress subscale of the Cumulative Adversity Interview administered at baseline and 6 months (9), that consisted of 62 items relating to the subjective experience of continuous stressors or on going life problems and hassles.

On a separate day from intake and baseline assessments and after overnight fasting, participants came to the laboratory at 7:30AM, at which time an intravenous line was inserted and four repeated samples of cortisol were drawn 15minutes apart over the course of 1 hour and then averaged across time points. In addition, circulating plasma total ghrelin, leptin, insulin, and plasma glucose levels were drawn once and tested in duplicate.

Morning cortisol levels, ghrelin, leptin, insulin, and chronic stress were used to predict changes in weight and the frequency of food cravings over the 6-month period.

## Results

This is the first prospective naturalistic study in a community sample that demonstrates that higher levels of fasting total ghrelin were predictive of future food cravings. These results suggest that ghrelin plays a role in increasing motivation and subjective craving for foods and in reward-based eating, particularly for complex carbohydrates and starches.

Ghrelin increases with fasting, peaking prior to meal ingestion, and decreases after eating. Peripheral administration of ghrelin promotes food intake and stimulates food intake by activating homeostatic hypothalamic circuits (10).

Neuroimaging studies have demonstrated that ghrelin administration increases the neural response to food pictures in areas associated with hedonic eating (i.e., amygdala, hippocampus, orbito frontal cortex, striatum, and ventral tegmental area (11).

Similar to some previous studies (12), we observed an inverse relationship between cortisol and BMI, as well as cortisol and stress, in cross-section alanalyses. However, higher baseline cortisol, chronic stress, insulin, and HOMA-IR(a measure of insulin resistance) predicted short-term weight gain over a 6-month period.

The results indicate that while morning cortisol may be blunted among individuals with higher BMI when examined in cross-section alanalyses, future weight gain may be related to complex feed-forward and feed-back HPA axis dynamics where in individuals may use food to regulate stress and HPA axis responses (13).

Cortisol also helps to regulate feeding behavior and choice (14). These results may be due to the direct effects of cortisol and insulin on lipid accumulation through activation of lipoprotein lipase (15).

Elevated cortisol stimulates gluconeogenesis, which can result in insulin resistance (16).

Cortisoli ncreases under the physiologic stress of mild hypoglycemia, which in turn increased brain activation in stress and reward motivation pathways and also increased wanting for high-calorie foods (17), higher insulin instead was associated with greater brain activation in reward regions in response to stress and to food cue exposure, but only in individuals with overweight (18).

These findings suggest that dynamic stress-related cortisol changes as well as adaptations in cortisol and insulin may modulate brain extrahypothalamic reward and motivation regions to influence future weight gain. Experimental studies are necessary to focus on the potential relevance of interventions

targeting stress and/or disrupted cortisol responses for weight management. For example, in a recent 8-week trial, 52 participants were randomized to placebo or treatment with ashwagandha, a standardized root extract that has been suggested to help counteract the negative effects of stress (19). Relative to placebo, treatment with ashwagandha resulted in significant improvements in perceived stress, food cravings, cortisol, and weight.
Several laboratory-based stress paradigms have beenused to investigate stress effect on eating and weight. chose to use the natural self-report of chronic stress participants and circulating hormonal measures while the participants were fasting. It is possible that different responses would be seen during acute or laboratory-based stress or feeding paradigms. The resultsi ncluded a prospective short-term (6-month) follow-up assessment for prediction of future food cravings and weight gain.
The longer-term effects of cortisol, stress, and appetitive hormones and their associated weight outcomes are unknown and longer follow-up studies are needed.

## Conclusion

In conclusion, ghrelin was associated with future higher frequencies of food cravings over the 6-month follow-up period, suggesting it srole in motivation for food and reward-base deating. Chronic stress, cortisol levels, insulin levels, and HOMA-IR each predicted future weight gain over the 6-month assessment period in a sample of adult volunteers recruited from the community. Future research is needed to test whether interventions targeting stress and disrupted cortisol responses may help to mitigate weight gain in community samples.

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## 22. Long-Term Weight Loss Maintenance: Analysis of Factors Responsible of Relapse Through the Biopsychosocial Model

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### Background

Relapse is a common problem following weight loss intervention(1). Behavioural approaches to obesity management often lead to clinically significant weight loss, generally regained(2) in short time: most of patients return to pre-treatment weight within 3 years(2). Multiple factors are responsible for obesity and eating disorders: individual (biological and psychological), social and cultural factors, all interactingwith each other and causing establishment and duration of eating disorders. A successful model should take in account all the aspects related to the problem.

From the 1960s to today, specific programs for obese patients have been developed to educate them to healthy eating and physical habits and to make them more aware during food intake.[7]In the early 2000s, Cooper et al[6] developed an alternative treatment for obesity integrating more specific cognitive behavioral strategies. As such, cognitive BT-OB (CBT-OB) was designed to address the disappointing longterm results of previous behavioral treatments through cognitive behavioral analysis of the processes responsible for weight regain.

### Hypothesis/Purpose

In this review, we aim to examine and compare different types of pre- and post- interventions to avoid relapse with a particular focus on predictive factors, specifically on the application of a different model. Today, the model used to explain the etiology of the obesity and eating disorders is the biopsychosocial model. The aim of the biopsychosocial model is to focus on the patient as a person, human being with thinkings and emotions and to help him to gain global wellness, where the weight management has a crucial role(3). This kind of approach improves the self-esteern of the patients and helps them to avoid relapse.

### Study Design

Systematic review of published studies.

### Methods

The review was assessed including eligible studies on weight regain and outcomes of the application of biopsychosocial model for the treatment of diseases.

### Results

Biopsychosocial approach did allow the clinicians to shift the focus from biomedical model to a more comprehensive approach. Scientific research has shown that treatment of eating disorders and obesity is successful in the long time(6–11) only if it is conducted according to a highly structured and multidisciplinary intervention model, which includes cognitive-behavioral therapy, interpersonal therapy, family therapy, individual and group psycho-education therapy. Cognitive Behavioural Therapy (CBT) is a

structured, short-term, present oriented psychotherapy used to modify dysfunctional thinking and behavior(4). CBT has been found useful in weight loss when CBT is combined with diet and exercise interventions when compared with diet and exercise alone(5). In their retrospective review, Nguyen et al.(4) showed that integration of biological, psychological and behavioural interventions can lead to up to 10,8 % weight reduction(4) over about 3 months of treatment. Dalle Grave et al.(12) followed 88 patients with severe obesity , treated with high-protein diet (HPD) o high-carbohydrate diet (HCD), in a randomized control trial. The treatment included 3 weeks of residential CBT. Weight loss at 43 weeks was 15% for HPD and 13,3% for HCD. The percentage weight loss achieved by these treatments was much higher than the mean 8-10% seen in conventional life-style modification programs, furthermore no tendency to regain weight was observed between 6 and 12 months(12).

## Conclusion

A multi-disciplinal approach that consider the patient not only on his biological/medical side seems to be the only successful approach to avoid weight regain after a treatment. Moreover, it is suitable for treating patients with severe obesity and associated medical comorbidities and disability, who are generally referred for bariatric surgery rather than attempting less invasive approaches.

Keywords: Weight relapse, biopsychosocial model, obesity, eating disorders

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## 23. Psoriasis: lifestyle and diet

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### Background

Psoriasis is a chronic immune-mediated disease that affects 3-4% of the world's population (Rachakonda TD et al., 2014). Following multiple studies, to date, it is possible to believe the system immune, both innate and adaptive, responsible for the pathogenesis of psoriasis, whose severity can be influenced by environmental factors such as smoking and emotional stress (Jankovich S. et al., 2009). Factor environment of great interest for these patients is the influence of nutrition. Popular literature, in fact, it contains many tips to be observed in the case of psoriasis, which is scientific literature limited. In fact, the strongest scientific evidence exists when weight loss is observed, mostly among them obese psoriatic patients (Bryld IF et al 2010; Wolk K et al 2009), and for gluten-free diets (GFD), able to reduce the effects of psoriasis in a subgroup of patients, ie those that exhibit specific antibodies for celiac disease (Bhatia BH et al., 2014; Michaelsson G. et al., 2007). Unfortunately, there are no studies that describe the real effects that popular recommendations on the diet have on patients. There limited literature on the diet to be observed in case of psoriasis is therefore a lack of important knowledge that makes it difficult for both patients and physicians to discuss this topic.

### Hypotesis/Purpose

Psoriasis is increasingly commonly referred to as a systemic inflammatory condition which manifests itself throughout the body, with rapid growth: try this, in support ofan association between psoriasis and cardiometabolic diseases, as well as various other comorbidities (Takeshita J et al., 2017). From these statements, it was recently possible to propose ed to encourage greater need to provide comprehensive assistance to psoriasis patients (Takeshita J et al., 2017). So, there is a need to engage with recommendations on nutrition and seek new management options for psoriatic patients for the purpose of moving to a complete care not only for control and for the prevention of their own skin disease but also for managing their overall health in the long run. To the to understand the role of the diet in the treatment of psoriasis, they were conducted surveys on patients affected with the following goals: (1) quantify the intake of a specific food in psoriasis patients compared to the rest of the population; (2) identify foods included among popular recommendations and check their influence on improvement of psoriasis based on the response that can be observed on the skin of patient; and (3) Understand the attitudes and perceptions of affected patients the role of the diet in managing the disease it self. Let's look at what foods are to be recommended to a psoriatic patient. It has been said that taking some nutrients can even aggravate the illness or become an element triggering, as, on the contrary, a vegetarian diet with few fats and few proteins can to make improvements. Considering that every psoriasis patient reacts differently and it can develop a hypersensitivity to a food rather than another, who is affected by it pathology should however eliminate or reduce drastically the foods they produce "heat", that is, very energetic ones, such as red meats, sausages, eggs, butter, margarine, fries, salt, seasoned cheeses, milk and derivatives, sugar, including alcohol and spirits. The mechanism of how each of these substances can induce or exacerbate psoriasis is unclear.

### Study design

However, previous studies have confirmed that these dietary components cause alterations in the intestinal microbiotic composition, irritate the intestinal mucosa and increase the stimulation of the immune system. Simple sugars taken in the diet can cause dysbiosis of the intestinal microbial, resulting in increased bacterial strains which stimulate the release of cytokines by the immune system (Sorensen LB et al., 2005; Spreadbury I et al., 2012). On the other hand, the most complex carbohydrates, characterized by a high The number of fibers, such as those found in fruit and vegetables, have the opposite effect on microbial intestines, as they reduce inflammation (Ajani UA et al., 2004; Suter PM et al., 2005). An increase in the number of inflammatory cytokines may also explain the existing link between alcohol of psoriasis. Excessive alcohol intake is, in fact, closely linked with the development of psoriasis and is related to the severity of the disease (Kirby B et al., 2008; Poikolainen K et al. 1994). The interaction mechanisms proposed between alcohol and psoriasis include an increase in proliferation of lymphocytes and over-stimulation of inflammatory cytokines (Ockenfels HM et al., 1996; Schopf et al., 1996). In addition to overstimulation of inflammatory cytokines, substances capable of damaging the intestinal lining, such as, for example, the beautiful woman can also help to exacerbate immune-related disorders. Belladonna is part of one family of plants called Solanacee, which includes tomato, potatoes, aubergines, tobacco, pepper and petunia, which can influence digestion and absorption of nutrients in beings
humans and animals (Cardenas PD et al., 2015). The beautiful woman produces alkaloids, which adversely affect the intestines of mammals and aggravate the disease (Patel B et al.,2012).

## Methods

Several studies have confirmed the coexistence of celiac disease and psoriasis, with the improvement of psoriasis lesions after initiating a gluten-free diet (Bhatia BK et al., 2014; D'Erme AM et al., 2015; De Bastiani R et al. 2015). The advantage of GFD lies in the ability to reduce the signs of psoriatic pathology in patients who are antidepressant antibody (Michaelsson G et al., 2003; Takeshita J et al., 2017). While some dietary elements are considered to be able to trigger psoriasis, other foods have been suggested to improve their symptoms. Most commonly reported include omega- 3 (which is poor in skin psoriasis) and polyunsaturated fatty acids (PUFAs) found in fish or oil (Millsop JW et al., 2014), fruits and vegetables, with added vitamin D and probiotics. However, there is no evidence of a symptom improvement following the assumption of fish oil supplements and omega 3 (Bittiner SB et al., 1988). PUFAs are believed to reduce conversion of arachidonic acid to leukotriene B4, which is elevated in psoriatic lesions (Jiang et al., 2016; Turini ME et al., 1994). In addition, PUFAs reduce the production of tumor necrosis factor (TNF) - Alfa, interleukin (IL) -1β, IL-1a, in healthy adults and in patients with rheumatoid arthritis (Caughey GE et al., 1996).

## Results

Other studies have suggested an inverse relationship between psoriasis and the intake of fruit and vegetables (Brown AC et al., 2004). Fruits and vegetables provide rich antioxidants such as carotenoids, flavonoids, vitamins and minerals that were inversely related to TNF-alpha, C-reactive protein (CRP) and IL-6 (Holt EM et al., 2009). Not all vegetables and fruits, however, are allowed psoriasis. Recent studies, in fact, have shown that eggplants, raw tomatoes, peperones raw and cooked, artichokes, berries, raw apples, kaki are to be avoided, while increasing the consumption of loving vegetables such as chicory, radicchio, bitter pumpkin, crescione. Vitamin D, like mentioned above, may have antiproliferative and immunomodulatory effects. While probiotics aim to restore balance with the guest intestinal microbial. Very useful, then, would increase the intake of water, up to at
least two liters per day, given that in psoriasis, as in skin diseases in general, the skin is dry. Water purifies, hydrates, nourishes the skin, helps to mitigate the "fire" of the skin. Another good rule to follow is that of keep your body weight within the so- called "weight form". It was, in this sense,

observed an appreciable improvement in symptoms in patients who, in therapeutic treatment Associated diets: Pagano, Paleolithic, Mediterranean, Vegan, gluten-free or protein-rich food regimes, and poor carbohydrates. In Particularly, a major improvement in psoriasis injuries has been documented in everyone patients who for 6 months have followed a diet similar to the Pagano diet, which involves a rise in fruit and vegetables and a decrease in the beauty of the skin and junk food among the others recommendations (Brown AC et al., 2004). An observational study showed a improvement in a subgroup of patients with psoriasis after a 2-week fast and one vegetarian diet during the next 3 weeks (Lithell et al., 1983). In addition, in patients with rheumatoid arthritis and atopic dermatitis, vegetarian and vegan diets have been shown to relieve the symptoms and promote weight loss, which may decrease mediastinal inflammation from adipocytes (McDougall J et al., 2002).

## Conclusion

*Psoriasis: Recommended nutrition*

The recommended diet for psoriasis is based on the consumption of:

- Foods rich in vitamin A (spinach, basil, asparagus, peppers, carrots, pumpkin, tomatoes, coral, liver, eggs and fish).
- Foods rich in omega 3 fatty acids (flaxseed and flaxseed oil, salmon, mackerel, sardines, swordfish, fish oil, nuts, eggs)
- Foods rich in vitamin C (orange, grapefruit, lemon, kiwi, apple, watermelon, garlic, celery, figs, aubergines)
- Foods with folic acid (whole grains, legumes, spinach, oranges, asparagus, lettuce, wheat germ)
  Foods rich in selenium (grapes, peaches, garlic, pumpkin, barley, oats, corn, pistachios, asparagus and spinach)
  White meat (turkey, chicken)
- Fresh cheeses
- Yogurt

According to some studies, the gluten free diet could help psoriasis patients, however at present, it is not possible to say that this food regime is realbenefit

*Psoriasis: foods to avoid*

- Among the foods to avoid in the case of psoriasis
- Fat meat
- Red meat
- Sausages
- Palm and coconut oil
- Trans fats (margarine, etc.)
- Butter
- Hard cheese
- Alcohol
- Fried
- Foods with preservatives and additives
- Spices too hot or strong

- Savoury Foods

To limit the consumption of too acidic foods (coffee, acetate and chocolate) seasoned cheeses, milk and eggs. Experts also recommend removing it completely also cigarettes and keep body weight under control.Obesity, in fact, is considered not only a risk factor for the the appearance of the disease, but also a deterrent to the cure, as would make patients less sensitive to therapy.Beyond the diet, the patient is also stimulated to adopt a healthy lifestyle and correct avoiding behaviors that worsen the state of the disease, such as scratching them injuries, use soaps, cosmetics, or irritating clothing (prefer cotton wool or fiber synthetic), exposed to low temperatures...
Although the debate is still open, we can say with certainty that it is enough to respect a few simple rules to improve the general health conditions of these patients.

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## 24. Fibromyalgia and Nutrition: Update on Diets and Supplements

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### Background

Fibromyalgia (abbreviated in FM and also called Atlas syndrome) is a diffuse musculoskeletal pain syndrome ,that is part of rheumatic diseases. They represent a very heterogeneous group of affections whose main characteristics are inflammation and pain. The most prevalent ones are rheumatoid arthritis (AR), spondylarthritis (SpA) and osteoarthritis (OA), but to these are added diseases of the connective tissue, bone, extra-articular rheumatism and, fibromyalgia *[Punzi L et al, McGraw-Hill Education Ed. 2014]*.
Fibromyalgia is described as a generalized form of extra-articular non-inflammatory rheumatism with an uncertain origin. It's characterized by chronic muscular pain, associated with rigidity, asthenia (decreased power), insomnia or sleep disturbances, with possible anxiety and depression disorders in part of the patients *[Ciauw Daniel J. 2014]*. It's not fatal in itself, but the chronic pain associated with it is persistent and debilitating. Most patients report that the symptoms don't seem to improve with time.
The diagnosis and clinical features of fibromyalgia are very controversial. Often they arrive late and after many medical checks because, being a set of symptoms, they are often misunderstood.
Many people, therefore, suffer from fibromyalgia without receiving effective treatment, perhaps due to diagnostic difficulties. They do not have a good quality of life and can't maintain normal daily activity.
Fibromyalgia predominantly occurs in adult female persons. The reason is not yet clear, but the female sex is certainly the greatest risk factor for fibromyalgia (male / female ratio 1: 9).
The exact cause of this disease is still unknown and Fibromyalgia is diagnosed only for the exclusion of other pathologies (differential diagnosis) and subsequent palpitation of the tender points (points that, by applying pressure, give a localized pain).
After the exclusion of other muscular, neurological or skeletal disorders, in fact, there are two elements that allow proper diagnosis of fibromyalgia:

- An accurate history from which it is deduced that the pain is spread symmetrically and lasts for at least 3 months.
- 18 key points palpation (tender points, located parallel to both sides of the body). In the Fibromyalgia patient are not inferior to 11.

Among the different hypotheses for its etiology, oxidative stress is one of the greatest possibilities. Additionally, it is added that painful symptoms may be associated with the decrease in some neurotransmitters, mainly dopamine and serotonin. Reduction, especially of serotonin, may explain depression and anxiety disorders that many FM patients suffer from *[fibromyalgia.it, 2017]*. However, you should always remember that fibromyalgia is not a psychiatric illness and anxiety problems make it worse but don't cause it.
For what concerns dopamine, instead, recently has been shown to be the central role of dopaminergic neurotransmission in perception of pain, therefore a decrease of this neurotransmitter probably contributes to the emergence of painful symptoms occurring in fibromyalgia *[Wood PB, 2008]*.

### Hypothesis

If we know where the disease is born, it is easier to think of possible solutions,then it is easy to understand how,currently,no definitive cure for fibromyalgia has yet been definedbut many therapeutic options for managing chronic pain are available.

Treatments are of various nature and current literature suggests a combination of different types of care to achieve the best results *[Auquier L. et al., 2008]*. With a multidisciplinary approach, combining pharmacological and non-pharmacological treatments,among which a prominent role, of course, covers nutrition.

Many drugs, such as NSAIDs, have been used but have not been successful. It should also be considered, all time, the set of side effectsthat these medications carry with them. More successful were the central muscle relaxants or anxiolytics, but have temporary efficacy, since after a slight attenuation of painful symptoms, they accentuate the cognitive and perceptive deficits often present in the syndrome. Recent studies have shown the efficacy of tricyclic antidepressants, as in the case of amitriptyline. The results seem discrete but have a short duration *[Sommer C, 2008]*.

Apart from antidepressant, amitriptyline, at low dosage, can be used to prevent some forms of headache and is also used in ankylosing spondylitis for pain therapy.

They have also been used:

- antiepileptics (such as gabapentin), which, unfortunately, give only appreciable results on a small percentage of patients.
- opioid central analgesics (tramadol and codeine / paracetamol), acting on pain routes
- but induce tolerance and dependence and the Food and Drug Administration does not approve of its use. *[MacLean, AJ. et al, 2008]*

Non-pharmacological treatment, however, provides for rest but without completely neglecting physical activity (not to aggravate the symptom of stiffness already present) that must be continuous but not excessively intense. Most important, then, is the recovery of lost sleep and undertake a proper diet.

It is precisely at this last point that research is focusing in recent years: finding a correlation between diet and fibromyalgia in order to create a sort of guideline for patients with FM.

## Study Design

From 2000 to 2015, an Italian group has decided to revise, through a systematic research done on Medline, current knowledge on the link between fibromyalgia and nutrition. The goal was to identify nutritional guidelines to support the patient during therapy and improve so its quality of life *[Rossi A, et al, 2015]*.

It has been shown that diet can affect the development of rheumatic diseases. It is able to interact with specific cellular activities by modulating the inflammatory process. The lifestyle and in particular way the diet may, in fact, affect the progression of inflammatory diseases.

The Mediterranean diet is definitely the most useful one.

The term "Mediterranean Diet" means a nutrition model inspired by Italian, Greek, Spanish and, in general, of all those nations that face the Mediterranean Sea, of the early sixties. The choice of that historical period and this geographical area is based on some scientific and epidemiological evidence *[WC. Willett et al., 1995]*. In fact, these countries share, more or less, the same foods and various studies widely accepted by the scientific community have proven that in these geographic areas life expectancy was among the highest in the world at that time, while the incidence of cardiovascular or tumor illnesses was among the lowest in the world *[Ancel B, 1980]*.

It is a diet that favors cereals, fruits, vegetables, and olive oil, compared to red meat and animal fats, with moderate consumption of fish, white meat, legumes, eggs and milk products.

The various components of the Mediterranean diet have shown a variety of beneficial effects. Fatty acids such as omega-3, oleic acid and polyphenols inhibit the production of proinflammatory substances and the activity of immune cells, with positive effects on clinical disease indexes *[Oliviero F et al., 2017]*.

Many of those foods, who are the protagonists of our table (like tomatoes, aubergines and peppers), however, contain pro-inflammatory molecules called glycoalcaloids (alcaloids with attached a sugar) slightly toxic. They can cause inflammation or worsen the FM, triggering inflammatory phenomena.

Among the irritants is also gluten, a lipoprotein that originates from the union of two types of protein: prolamine (gliadin for wheat) and glutenin. They are mainly found in cereals such as wheat, spelled, rye and barley. Gluten-sensitivity is a disorder completely different from celiac disease, but it creates an inflammatory reaction in the body that could worsen an FM already present. Therefore, the elimination (or reduction) of gluten from the diet of these patients can be considered a potential dietary intervention that can lead to clinical improvement *[Rossi A, et al, 2015]*.
Also, obesity and overweight, very common in these patients, are related to the severity and aggravation of the disease.
The visceral fat tissue seems to be the most dangerous type of fat for health because it is more associated with cardiovascular risk, insulin resistance *[McCarty MF. 2003]*, type 2 diabetes, various metaboliccomplications *[Pouliot et al. 1992]* and arteriosclerosis *[Vague et al. 1980]*. Weight control is therefore a very effective tool for improving symptoms and quality of life.
Are available various other information, even not strictly scientific, regarding the benefits of nutrition in FM cases.
The Mediterranean diet, however, is not the only viable route. Laura-Isabel Arranz*[Arranz, Laura-Isabel et al. 2010]* carried out a study aimed at discovering what is actually known by various scientific studies concerning fibromyalgia and nutritional status, diets and dietary supplements. The research was carried out in 2009, for articles published between 1998 and 2008, and this study has shown how vegetarian diets have the most beneficial effects on FM, probably due to increased antioxidant intake and to the reduction of proinflammatory phenomena.
The vegetarian diet, especially vegan in its crudest variant, has proven to be an effective form of treatment, at least in the short term, for fibromyalgia *[Donaldson MS et al. 2001; Kaartinen, K et al. 2000]*.
Obviously there is no specific diet to be respected in the case of fibromyalgia, but that does not mean that, to fight pain and fatigue, a proper eating habit plays an important role. Many patients reported an improvement in symptoms during low-fat diets. Food counseling can be summarized as follows:

- Reduce sugar, especially if refined.
- Limit the consumption of red meat and prefer other sources of animal protein.
- Eat lots of fresh fruits and vegetables of season, for the intake of mineral salts and vitamins.
- Reduce the use of salt and drink plenty of water.
- Limit the use of coffee and tea.
- Avoidalcohol.

An agglutinate and normoproteic diet, supplemented by alkalinizing agents, vitamins, and various nutraceuticals, is the most effective therapeutic protocol for the treatment of fibromyalgia. Such therapy is able to reduce drastically the thickness of visceral fat and insulin resistance, resulting in a decrease in the production of inflammatory substances.

## Methods

Basedon what has been said so far, we have focused on the correlation between diet and inflammation reduction in order to alleviate the symptoms of fibromyalgia.
For this reason we have pursued a systematic research on the main scientific disclosure sites: PubMed, Scopus, ResearchGATE and Google Scholar. The searches were carried out with the keywords: Fibromyalgia, Nutrition, Diets, Supplements, Nutraceuticals.
From this, we have put together a number of extremely useful data that have only proven our hypothesis.

## Results

It has been observed that the prevalence of rheumatic diseases in southern European populations is lower than that of the rest of the industrialized countries. These differences, as we have seen, have been attributed, at least in part, to dietary factors, first of all the wider consumption of olive oil and fish, as well as greater adherence to the Mediterranean diet. The risk of developing these pathologies is inversely

proportional to the consumption of olive oil *[Linos A et al., 1999]*and nd fishwith high content of "good" fat *[Pedersen M et al., 2005]*.

Therefore it's evident that eliminating certain substances from the diet, it can avoid the worsening of the symptomatology of fibromyalgia, if not even to determine its improvement.

From this it can be seen that, just like the elimination of certain substances, food supplementation can also have a positive influence on clinical progression. Those nutrient principles contained in foods that have beneficial effects on health are called nutraceuticals. The Ministry of Health defines nutraceuticals as "a food that, thanks to the content of particular constituents, is able to claim a beneficial effect on a specific function of the organism".

They are normally found in nature, but their percentage is almost reset from the industrial processes that food undergoes. Nevertheless, they can be extracted, synthesized and used as food supplements or added in foods.

Regarding their beneficial role, there are fewer scientific evidence in the literature than the diet, but they have shown important anti-inflammatory effects even if their use in rheumatic diseases is still limited. The study of the role of nutraceuticals in rheumatic diseases has received considerable impetus over the last 20 years. Various dietary compounds have, in fact, shown important effects on specific cellular activities involved in the release of inflammatory mediators and oxidative stress. Most of these, such as olive oil polyphenols, and the omega-3 fatty acids present in the fish, we have already seen that they are part of the Mediterranean diet,to which the most important beneficial properties are attributed. The various formulations of commercial nutraceuticals are based on the compounds listed and their administration is recommended for cycles of a few weeks repeated over time.

It has been shown how also the integration of vitamins and mineral salts has benefited in FM patients. Food supplements are defined as "foodstuffs intended to supplement the common diet and which constitute a concentrated source of nutrients such as vitamins and minerals or other substances having a nutritional or physiological effect, in particular but not exclusively, amino acids, essential fatty acids, fibers and plant extracts, both monocomposed and multi-composite, in pre-formed forms. "

Many nutritionists agree that supplements are rightly recommended in cases where the body has a real shortage of certain elements. However, you have to keep in mind that they are not healing substances and only serve to supplement a normal diet.

They are normally used in sports or in a context of severe debilitating stress, but their "offlabel" use has led to various benefits. In the study of Kathryn D. Dykman*[Dykman K.D. et al. 1998]*, fifty subjects were diagnosed with fibromyalgia and / or chronic fatigue syndrome (CFS). Everyone had received some form of medical treatment before taking nutritional supplements and every subject was interviewed both before the study than after nine months.

With medical treatments, about 25% of patients affected by FM has improved, but the beneficial effects of treatment rarely persisted for more than a few months. Food supplements have determined a significant reduction in the severity of the initial symptom and the subjects who received both treatments persisted in remission for a longer period of time.

Supplements most commonly used are vitamin supplements, especially vitamin B complex supplements (vitamin B12 in particular), vitamin D3 and malic acid. Other sources indicate how also supplementation with vitamin C is able to improve these issues *[Richardson, J et al. 1983]*.

Also magnesium supplements allow you to draw a large number of benefits. It is involved in several functions that affect the body. It is responsible for the contraction and relaxation of the cardiac and skeletal muscle. And its lack can lead to muscle spasms, heart failure, confusion, tremors, weakness, personality changes, apprehension and loss of coordination. It helps the body metabolize carbohydrates and is able to influence the production of insulin levels. The bond between magnesium and insulin makes the presence of this mineral an even more important factor for people with type 2 diabetes. Patients presenting this condition and which have low levels of magnesium can benefit of magnesium supplements and thus obtain better regulation of mineral levels and at the same time of insulin levels.

Other active ingredients possess properties useful for improving the depressive state and sleep quality, lessening the pain and feeling of fatigue [Boschiero, D, et al 2015]. They are:

- Tryptophan. Since the human organism is unable to synthesize it,must be obtained from foods and therefore is classified among the essential amino acids. In nature it is found in animal protein. It is involved in numerous chemical reactions, particularly in the synthesis of serotonin and nicotinic acid. For many people it has proven to be a fairly effective and safe remedy to promote sleep, as it increases serotonin levels in the brain. It has been promising as an antidepressant and another possible indication seems to be the attenuation of chronic pain.
- Melatonin. It is a hormone produced by the pineal gland. It acts on the hypothalamus and has the function of regulating the sleep-wake cycle. It is essential for regulating seasonal and circadian biological rhythms, improves sleep, has sedative, ansiolytic, antioxidant and antiaging properties.
- L-Carnitine. It is an amino acid derivative, used for several years as a nutritional supplement. It is synthesized in the human body, predominantly in the liver and kidney, starting from two amino acids, Lysine and Methionine, in the presence of Niacin, Vitamin B6, Vitamin C and Iron. It is contained mainly in animal foods such as meat and milk products. Its administration detects a progressive improvement in skeletal muscle mass and a simultaneous and significant reduction in muscle fatigue. In the body, the concentration of carnitine tends to decrease in parallel with loss of skeletal muscle mass. The most well-known activity of carnitine is its role as a long chain fatty acid transporter in the mitochondrial matrix, whereby fatty acids are converted into energy through the Beta-Oxidation process. Its administration, in fact, stimulates a reduction in adipose tissue, an improvement in skeletal muscle mass and physical and cognitive capabilities as well as reducing fatigue [Malaguarnera, Mariano et al. 2007].
- S-adenosylmethionine (SAM). It is a coenzyme involved in the transfer of methyl groups (a processdefined methylation). It is the active ingredient of a well-known drug marketedin Italyunder the name of Samyr, which belongs to the class of C class antidepressants (ie the patient's total burden) while in the United States it is considered a food supplement. S-Adenosil Methionine has been tested in the treatment of various pathologies (especially depression, osteoarthritis and liver disease).
- Coenzyme Q10 (ubidecarenone or ubichinone). It is a molecule of the ubichinone group, liposoluble benzoquinones involved in the transport of electrons in mitochondria and cellular oxidative phosphorylation. The progressive decrease in CoQ10 is a condition that is particularly controlled during statin treatment and is the cause of muscular pain that often pushes the patient to reduce the dose or suspend the therapy [DiNicolantonio, J.J. 2012]. Nonetheless, several studies focus on the relationship between reducing Q10 coenzyme levels in muscle cell mitochondria and myalgia.
- Omega 3. Many omega-3 compounds, many of which contain Omega-3, Omega-6, Omega-3 precursors mixed with each other or with vitamin-based compounds, can be found on the market, all of these compounds belong to the category of dietary supplements .

**Conclusion**

So, how to cure Fibromyalgia? Some tips might be:

- Reduce carbohydrate-rich foods that can increase intestinal fermentation.
- Restrict animal proteins, coffee, tea, refined sugars and spirits: prefer fruit, vegetables and whole grains [Busch AJ, et al, 2008]
- Vitamin B12 is crucial in all patients with FM because it significantly reduces inflammation.
- Vitamin C is very important in all subjects suffering from chronic pain because of its antioxidant and regenerating effect on the connective tissue.
- Optimize Vitamin D Values

- Magnesium is very useful in restoring cellular energy production functions. I treduces brain neurotoxicity.
- Tryptophan (precursor of some brain neurotransmitters) has shown in clinical studies to reduce the symptoms of FM.
- Melatonin. Powerful antioxidant, improves the health of mitochondria and the production of ATP (energy). It has proven to be very useful in the treatment of fibromyalgia in several clinical trials. It reduces the activation of the cerebral microglia (immune system).
- Acetyl-L-Carnitine. It plays a critical role in improving mitochondrial production of ATP.
- Coenzyme Q10: Patients who take it see the symptoms (pain and headache) significantly reduced.
- Assess the use of omega 3 anti-inflammatory drugs.

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## 25. Ketogenic Diet for Children with Epilepsy

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**Abstract**

A ketogenic diet (KD) is a dietary approach to treat intractable epilepsy. The KD begins with hospitalization of child and their parents can adapt to the KD for 1-2 weeks. Recently, various type of dietary intervention such as the modified Atkins(MAD) diet and the low glycemic index treatment (LGIT) have been performed. Since 2010, they carried out the KD, MAD, and LGIT for total of 802 patients; 489 patients (61%) for the KD, 147 patients (18.3%) with the MAD, and 166 patients (20.7%) for the LGIT. In this report, application of these dietary practices in is shared.

**Introduction**

Since 1920, the ketogenic diet has been recognized to be effective in the treatment of childhood epilepsy. After the introduction of anticonvulsant drugs, interest in treatment based on the ketogenic diet decreased until 1990 when subsequent clinical trials and studies demonstrated its practical utility in many situations.

Various studies have been conducted to understand its mechanism of action in epilepsy, and various hypotheses have been advanced:

- a direct anticonvulsant effect of ketone bodies;
- a reduced neuronal excitability induced by ketone bodies;
- an effect on the target of rapamycin in mammals;

**Thesis**

In 2008, the efficacy of a ketogenic diet was demonstrated in a murine epilepsy model, and that the protection from the crisis was not linked to the level of ketosis in the blood, indicating the need for further studies on the role of ketone bodies in the " epilepsy.

Although the mechanism of action is unclear, the ketogenic diet is now considered a consolidated part of an integrated approach, along with pharmacological therapy, in the major centers for epilepsy worldwide . An important advantage is the reduction of drug use and the reduction of serious side effects often associated with antiepileptic agents.

The efficacy of ketogenic diet is strongly supported by a recent review by Cochrane in which all studies showed a 30-40% reduction in attacks compared to comparative controls, and that in children the effects were comparable to modern antiepileptic drugs.

The KD can be traced back to the texts of Hippocrates at the 5th century BC. Wilder (1921) reported significant seizure control effect of the KD at first The KD is composed of high fat, moderate protein and restricted carbohydrate and it results in a state of ketosis. The most frequently used ratios of fat to non-fat (carbohydrate + protein) in the KD diet 4:1 and 3:1. To maintain strong ketosis state, 4:1 ratio isused and 3:1 ratio is used for under 1 year or older children to improve compliance with the KD. In order to maintain the 4:1 ratio of fat and non-fat (carbohydrate + protein), large amount of fat is needed from oils not only from the fat partially contained in a certain.

The carbohydrate-rich foods such as rice, bread, grain and simple sugars are eliminated. One food is selected from each food group which is categorized to either meat, fish, vegetables, milk or fat

sources. The amounts of each food are calculated in grams and the content of nutrients are analyzed to achieve a desired ratio based on the individual nutrient requirement. It is not easy for caregivers to calculate the amounts of each food in grams by themselves. For their convenience, the KD team provides them a computer program to calculate accurate amounts of foods and nutrients contents to minimize human errors. After calculation, the proportions of carbohydrate, protein, fat in calories, the desired ratio, and nutrient requirement of a patients are confirmed The meals are provided in accurate amounts by weighing food with digital precision scale.

Based on the tricarboxylic acid mechanism, the ketogenic diet is an appropriate first-line therapy for patients with seizures associated with metabolic disorders such as glucose transporter protein deficiency (ie, De Vivo disease) and pyruvate dehydrogenase complex deficiency.7 Another indication for the ketogenic diet is intractable childhood epilepsy.

**Conclusion**

In conclusion, the role of ketogenic diet in the treatment of epilepsy is well established and we are confident that this also affects weight loss, cardiovascular disease and type 2 diabetes; an improvement of risk factors such as weight, saturated fat, inflammation: this should encourage continuous work on the therapeutic value of the ketogenics diet.

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## 26. The Ideal Pattern of Lipids in Long-Time Ketogenic Diets

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**Background**

Ketogenic Diet (KD) has been employed for medically refractory epilepsy for almost a century. Furthermore, KD is currently used as first choice therapy for GLUT1 Deficency Syndrome and is also used for other metabolic pathologies such as the PDC Deficency and obesity. Possible uses for neurodegenerative pathologies, some types of cancer and some post-traumatic brain damages are currently underway. A KD is generally defined as a high-fat, low-carbohydrate and moderate protein diet. Consisting of 70%-90% of energy from fat, KD can cause early and/or late adverse effects, such as dyslipidemia, consisting of increased triglycerides and/or cholesterol, leading to concerns about the increased risk of cardiovascular diseases (CVD).

**Purposes**

This study aims to hypothesize an ideal lipid pattern for long-time KD based on literature review analyzing fats properties and their roles on health.

**Results**

The classical KD is based on a ratio of fat to carbohydrate and protein, usually 3:1 or 4:1. The fat component is provided by long-chain triglycerides (LCT) which are contained in animal fats (pork, beef and eggs), vegetable oil (sunflower and safflower oil) and human breast milk. It is firmly established that LCT consumption increases total cholesterol and low-density lipoprotein cholesterol (LDL-C) and leads to higher levels of triglycerides (TG). A modification of this diet uses medium-chain triglyceride (MCT) as an alternative fat source. MCT are present in palm shell oil and coconut oil, almonds and butter. MCT yields more ketones per kilocalorie of energy than its long-chain counterpart, it is absorbed more efficiently, and is carried directly to the liver in the portal blood. This increased ketogenic potential means less total fat is needed in the MCT diet, allowing inclusion of more carbohydrate and protein. Most studies comparing the effects of saturated fats to unsaturated fats have focused on fats that contained a large proportion of their fatty acids as LCT. Very few clinical studies have examined the impact of MCT on CVD risk factors. Some of these studies show that long-term consumption of moderate amounts of saturated fats, in the form of MCT, does not have adverse effects on CVD risk factors. These results thus suggest discrimination between long-chain saturated fats, which have repeatedly been shown to result in higher TG and LDL-C concentrations compared to unsaturated fats, and medium chain saturated fats. Studies' results show that MCT consumption (12-20% of energy intakes) leads to comparable effects on CVD risk factors as an equal amount of olive oil, monounsaturated fat-rich, an oil considered to have beneficial health effects. Use of the MCT diet is less common and sometimes limited by the unpleasant gastrointestinal side effects with consumption of high concentrations of MCT oil. A decrease of the CVD risk factors can be achieved by the partial substitution of saturated fat-rich foods with unsaturated fat-rich foods (mono- and polyunsaturated fatty acids). The oleic acid is the most important among the monounsaturated fatty acids and occurs in various oils (i.e. olive oil), in many animals fat and in dried fruit. It facilitates the normal conservation of the hematic fluidity and reduces the LDL quota while it doesn't have significant effects on the TG and HDL levels. A quota of KD has to be reserved to polyunsaturated fatty acids (PUFAs), of which the most

known are the linoleic acid (safflower, grape seed oil), the linolenic acid (fat-rich fish, nuts and some vegetable oils) and the arachidonic acid (meat, fish and eggs). PUFAs such as DHA, AA, or EPA are believed to affect profoundly cardiovascular function and health. Importantly, one report documented that the rise (or drop) in total fatty acids during KD treatment closely paralleled clinical improvement (or loss) of seizure control. These findings suggest that KD-induced elevations in PUFAs such as DHA and/or AA might act directly to limit neuronal excitability and dampen seizure activity.

## Conclusions

An excessive use of saturated fats can lead to an increase of cardiovascular risk factors. Therefore an integration with mono- and polyunsaturated fatty acids should be included in the shared protocol for long-time KD patients. Considering the benefits and the adverse effects of lipids the ideal lipid pattern could be: saturated fats about 25% of total calories (including 15% MCT); MUFAs about 50%; PUFAs about 25% of total calories.

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### 27. Ketone bodies as an alternative energy substrate for improving exercise performances


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## Background

Low-carbohydrate-high-fat (LCHF) diets have been used as a means of weight loss and control of symptoms inseveral clinical conditions. LCHF induces blood ketone bodies synthesis, ketone bodies represent an alternative energysubstrate, and may alter substrate metabolism undercertain conditions such as starvation and aftersupplementation.

Long-term LCHF dietary intake may help control body weight and fat mass whilemaintaining lean body mass in athletes in weight-sensitive sports. Ketone bodies can serve as an importantenergy substrate under certain conditions, such as starvation, and can modulate carbohydrate and lipid metabolism.

Dietary strategies to increase endogenous ketone bodyavailability require a LCHFdiet for about 4 days to inducenutritional ketosis. However, a LCHF diet may impair exercise performance viareducing the capacity to utilize carbohydrate, which formsa key fuel source for skeletal muscle during intenseendurance-type exercise.

These metabolic changes may also prevent the decline in performance in later stages of repeated high-intensitymovements, in which the aerobic metabolism becomes more important. However, elevated blood concentrations of non-esterified fatty acids and ammonia during exercise after LCHF diets may lead to early development of central fatigue. Itappears that at least several months of adaptation to a LCHF diet are required for the metabolic changes and restorationof muscle glycogen to occur.

## Hypothesis/Purpose

The purpose of this study was to investigate if the ketone bodies can improve the exercise performances.

## Methods

Review of papers

## Results

The influence of ketone bodies on fuel metabolism duringexercise is unclear, in part because much of the availableinformation on ketone body kinetics has been obtainedfrom voluntaries subjected to prolonged fasting/starvation.Many studies have shown that consuming aLCHF diet over months or years does not lead tometabolic imbalances or serious adverse effectsprovided that it supplies sufficient energy andadequate amounts of protein. Contrary to the popular concept that dietshigh in fat would increase the risk for obesity,cardiovascular disease, and diabetes, severalmeta-analysis and systematic reviews documentthat long-term LCHF diets actually reduce thesemetabolic risk factors. Ketone bodies can be readily oxidized as afuel source by skeletal muscle during exercise, andhave a similar respiratory quotient to that of glucose (AcAc= 1.0, b-OHB = 0.89) if completely oxidized. By serving asan alternative fuel substrate, ketone bodies may reduce thereliance on glucose utilization and spare endogenousglycogen stores. Ketone bodies have been reported to improve metabolicefficiency, but there are currentlylimited human data available on the effects of ketone. Professional cyclists typically rely on carbohydratesupplements during prolonged multiday stage race. In this respect, a reduction inthe reliance on carbohydrate metabolism by supplementingketone esters, may improve performance. Sparing endogenous carbohydrate stores would, intheory, result in an increased performance capacity duringthe key parts of the exercise. Hypothetically, ketone body

oxidationmay also permit relatively higher exercise intensitythroughout the whole competitionbodies on exercise metabolism. Collectively, ketone body supplementation may provide analternative fuel source for working skeletal muscle and alterfuel selection during exercise. However, whether ketonebodies "spare" carbohydrate reserves or impair carbohydrateutilization during higher intensity exercise is unclear. Similarly, whether supplementation with ketone bodies canincrease the utilization ofIMTAG asfuel or attenuate lipolysisand the availability of FFA during exercise remains to be elucidated.

## Conclusions

Long-term LCHF diets appear to be safeand may even improve several metabolic riskfactors for chronic diseases in the generalpopulation. LCHF diets provide a promising wayto help control body weight and fat mass whilemaintaining lean body mass in athletes engagedin weight-sensitive sports. There is emergingevidence that LCHF diets could be beneficial,particularly for performance in ultra-endurancesports. Their effect on field-based sports thatrequire repeated high-intensity activities is alsopromising. It appears that at least several monthsof adaptation to a LCHF diet are required for themetabolic changes and restoration of muscleglycogen to occur. However, some aspectsregarding the effects of long-term LCHF diets inathletes are still unexplored and in need ofinvestigation, including:

1. Strength, power, psychologicalstatus, and perceptual-motor performance afterweight loss, especially in weight-categorizedsports such as wrestling, judo and taekwondo.

2. Performance in repeated highintensity exercise in field-based sports such assoccer and basketball.

3. The development of centralfatigue during endurance events.

4. Perceptual-motor performanceduring prolonged intermittent sports such astennis and soccer.

5. The ideal composition ofsaturated, monounsaturated and polyunsaturated

fatty acids in LCHF diets.

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## 28. Chemical and nutritional characterization of *Chenopodium pallidicaule* (cañihua) and *Chenopodium quinoa* (quinoa) seeds


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**Background**

The Andean people selected before of the Spanish conquest, a considerable number ofplants for food purposes. In their vast empireIn fact, the Incas had developed agricultureextremely diversified, suitable for the remarkable varietyof ecosystems and able to meet the needsfeeding a population of about 12 millionof the people living there. Some of the cultivated plants, such asmaize, potato and tomato were importedfrom the Spanish conquerors and found fast and widediffusion, so as to change the eating habitsand agriculture in Europe and later in the rest of the worldworld. It was not the same for many others who, disdainedfrom the "conquistadores", went irreparablylost and their agriculture fell into disuse.Also, like quinoa and other seeds and tubersandin, continued to be cultivated, consumedand marketed in the markets of small villageson Andean highlands.

**Hypothesis/Purpose:**

Quinoa (Chenopodium quinoa Willd.) Is an original cereal of the Andean Cordillera. Traditionally it grows in arid and semiarid lands and has a large genetic variability with more than three thousand ecotypes. It also presents an ability to adapt to adverse climatic and climatic adversities different heights; from 4000 meters altitude to the level of sea. Quinoa is a strategic alternative food and potential to solve the protein decifit in many populations of the world.

**Results**

Quinoa (Chenopodium quinoa Willd.) and cañihua (Chenopodium pallidicaule Allen) are native Andean food plants of high nutritional value used as food by the Incas and previous cultures. An extensive analytical study was done on three samples for each species for all amino acids, sterols, fatty acids and mineral determination. The aim was to evaluate the chemical and nutritional characterization of cañ ihua and quinoa in relationship with wheat, corn, rice, rye, as sources of dietary fiber and other bioactive compounds in human and animal. *C. quinoa* and *C. pallidicaule* present an excellent nutritional value with high (14-18%) protein content, balanced amino acid composition, trace elements and vitamins and contain no gluten. This food species presented rich flavonol and triterpene glycosides fractions that include different compounds. *C. quinoa* and*C.pallidicaule* are an excellent example of functional foods that aims to prevent the risk of various diseases.In pseudocereals, such as quinoa, albumins andglobulins are the major protein fraction (44–77%of total protein), which is greater than that ofprolamins (0.5–7.0%). Quinoa is considered to bea gluten-free grain because it contains very littleor no prolamin. Quinoa provides a nutritional,economical, easy-to-prepare, flavourful food sourcewhich is of particular relevance for people withgluten intolerance, such as those with celiac disease.

**Conclusion**

The chemical composition in proteins, lipids and carbohydrates can be compared to that of cereals more common as wheat and corn. Protein content (15%) is very interesting as well as the nutritional value of proteins, with good content in essential amino acids and with high values found for lysine, sulfurated amino acids and aromatic amino acids. The high content of polyunsaturated fatty acids (72.5%), compared to those defined as saturated (22.8%), recommended and searched for all foods, can ensure good activity in prevention hypercholesterolemia and cardiovascular disease.

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## 29.Effect of Ketogenic Diet on Overweight Patient. Alteration of Body Composition: FM, FFM and Idratation measured by Bioeletrical Impedance


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**Background**

Recent years have shown increasing interest in pediatric neuropsychiatry, neuropediatricians, epileptologists and general neurologists in the use of ketogenic diet (KD) for the management of epilepsies and for obesity management, which is a serious public health problem that is reaching epidemic proportions in Western countries

And it is a major risk factor for cardiovascular disease and multiple chronic conditions

Including hypotension, hyperlipidemia. The focus is on the fact that ketogenic diet is much less toxic than some of the drugs currently used, especially in the treatment of epilepsy .

Usually the body uses carbohydrates (such as sugar, pasta and bread) as fuel, but as the ketogenic diet or the VLCKD is very poor in carbohydrates, fats become the main fuel and require accurate calorie measurements, Liquids and proteins

- Ketone bodies are not harmful. They can be found in urine, in the blood and in the breath. Ketone bodies seem to have a direct effect on crisis control: at their high concentration there is a greater therapeutic efficacy of the diet.

**Hypotesis/Purpose**

Primary objectives of ketogenic diet are rapid weight loss, good body and muscle definition and more. Most studies show that this diet has a solid physiological and biochemical basis that is capable of inducing effective weight loss and improvement of various cardiovascular risk factors, visceral fat, insulin resistance, hormone control etc..This review summarizes current knowledge on various issues related to its use. The aspects discussed in some details include (I) monitoring the hydration state in the first few weeks, during a weight loss regimen using VLCKD protocol or anyway with ketogenetic protocol. (II) consensus and dispute over the ways in which the diet begins and different implementation protocols; (III) contraindications and side effects (such as headaches or nausea or dryness and constipation); IV) Subjects with BiVA with the history of water and nutrition and urine color to control the hydration status in two groups: one under tight control in how much and when to drink, the other branch instead Free of charge .V) data on efficacy . (VI) methodological aspects related to the evaluation of the clinical effects of diet and prospects for future research.

**Study Design**

Cohort study

**Method**

Retrospective Cohort study was utilized; a cohort is based on studies on the uselfulness of ketogenic diet, deepens how it can be used in which way it involves changes in body composition. It has been seen that the level of idratation is crucial, and where not balanced, there could be physical damage.

**Results**

Overall, the data examined show that considerable progress has been made to understand the ways of action of the diet, its efficacy and tolerability profiles, and its potential role in the various types of epilepsy. Although clinical trials carried out to date have important methodological limitations, several randomized and prospective study protocols have been recently proposed and are being implemented. The results of these hopes will provide highly sought-after high quality information to better define the role of diet in many patients, especially in obese.

## Conclusion

Changes in body composition from VLCKD especially on fat mass, free fat mass and changes in hydration during treatment after treatment based on literature data and some data reported by patients undergoing treatment. The ketogenic diet is an effective and safe medical treatment for even epilepsy, but must be carefully applied and monitored.

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**30. Observation and multidimensional evaluation of psychological characteristics relevant to eating disorder and their possible evolution in patients with obesity in treatment with a sequential cycle of ketogenic and mediterranean low calorie diet with ashwagandha root.**

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## Background

Chronic stress has been associated with many illnesses, including obesity. Chronic stress may also lead to changes in eating behavior eliciting craving and overeating. The relationship with food is related to the emotional state of the patient; eating behaviors can take forms ranging from dysfunctional eating behaviors to eating disorders. In addition, after a restrictive diet, a subject with multiple risk factors can develop eating disorders.

## Hypothesis

This study focuses on the observation and multidimensional evaluation of psychological characteristics relevant to Eating Disorder and their possible evolution in obese patients in treatment with a sequential cycle of ketogenic and Mediterranean low calorie diet with Ashwagandha support.

## Study Design

Case-control studies on subjects with obesity.

## Materials and methods

A group of 16 patients in treatment with a sequential cycle of chetogenic diet (28 days) and Mediterranean low calorie diet were randomized to receive either Ashwagandha root extract (500mg) twice daily or only diet therapy without Ashwagandha.

All patients completed the Eating Disorder Inventory III (EDI III) , the most used self-report questionnaire in nutrition research and clinical settings to evaluate the psychological traits in the diet and to assess the symptoms and psychological features of eating disorders concerns. It was completed in two steps:

T0: before starting diet therapy

T1: at the end of the full cycle

The first (T0) psychological encounter with the patient was preceded by a brief clinical interview during which the questionnaire was presented as a measure of their attitudes, feelings and behaviors related to food and other general areas, the subject was informed that there are no right or wrong answers and there is no time limit to respond. The questionnaires were completed individually in the presence of the psychologist. All items were analyzed and the scoring average was calculated for each scale to investigate the psychological profile.

## Results

At T0 both groups of patients are placed in the range of EDI "typical clinical range". This reflects a significant level of anxiety related to a wide range of psychological constructs and the presence of a dysfunction in personal and interpersonal psychological domains.

At the end of therapy (T1) reduction in body weight and BMI was observed in all patients, but the group of patients in treatment with Ashwagandha root extract reported lower scores in the general psychological scales of EDI III that include self-esteem(29 to 23), personal alienation(38 to 24),

interpersonal insecurity(35to27), interpersonal alienation(37 to 30), interpersonal deficits(36 to 24), emotional disregard(33 to 25), perfectionism (51 to 47), asceticism (53 to 50) and fear of maturity(56 to 45).

## Conclusion

The tendency to think and put in place short periods of loss of control and worry about diet, weight, and body shape had decreased. Ashwagandha may provide a potential additional benefit to support the diet.

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## 31. Association between Ketogenic Diet, Ashwagandha and Psychological Support in improving Fibromyalgia Syndrome

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### Background

Fibromyalgia is a constantly growing chronic inflammatory disease with an inadequate therapeut response (1). Fibromyalgia, also called fibromyalgia syndrome (FS), is a complex idiopathic rheumat disease. There are absent signs of blood, muscle, neurological and radiographic alterations; bod inflammation parameters are normal, but perception of pain by the patient is multiplied. It is prevalent adult female subjects (from the second to fifth decade), although there are rare cases of fibromyalgia pediatric age. It affect 2-8% of the population, with female incidence in male of 9:1. Often the diagnos arrives late and after many medical checks, or it can not be diagnosed with up to 75% of affected people (2 The fibromyalgia is accompanied mainly by muscle-tendon pain, asthenia, not restored sleep, memory an concentration difficulties (1). There is a close correlation between fibromyalgia, insulin-resistance an stress, so that phytotherapy feeding and supplementation, combined with psychological support, are a optimal means for these patients (2-4). The Aglucidic Nutrition Therapy controls the insulin-resistanc leading to a significant improvement of the index HOMA (2). Ayurvedic medicine provides us with a natur remedy: the ashwagandha, able to control stress levels by modulating the synthesis of cortico-adrenal hormones (5-6). The diagnostic criteria chosen for the clinical evaluation of the fibromyalgic patient wer two tests: the Scale of Pain, the Widespread Pain Index (WPI), and the Symptom Severity Scale, th Symptom Severity Scale Score (SS-Score).

### Hypothesis

Aim of the study is to evaluate the synergic effects of a normoproteic Aglucidic Nutrition Therapy (TNA combined with psychological support and phytotherapy on pain reduction, fatigue and memory an concentration difficulties.

### Study Design:

Case-control studies on subjects with fibromyalgia diagnosis

### Materials and methods

23 patients were divided into two groups and underwent a 28-day carbohydrate-free diet. The experiment group was given a supplement of ashwagandha (891 mg/day) and a short psychological support (totally sessions) not supplied to the control group, which received only the TNA. At time 0 and after 28 days th patients were subjected to the WPI and the SS-score in order to evaluate the reduction of the analyze symptoms.

### Results

The control group had a significant improvement in WPI of 59.1% ($p < 0.05$) and SS-Score of 46.3% ($p < 0.05$) while the experimental group, which took the ashwagandha and the psychological support, had a further improvement of 63.6% ($p < 0.001$) and 54.9% ($p < 0.001$) respectively.

## Conclusion

The study has demonstrated the efficacy of normoproteic Aglucidic Nutrition Therapy in solving th problems of fibromyalgia, but also a further enhancement of effective therapy with the use o ashwagandha and the psychological support.

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## 32. Man with Insulin-Resistance and Oligoasthenospermia: Case Report

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### Introduction

Male infertility is a worldwide growing problem. Male infertility corresponds to a reduced reproductiv capacity of men, due to an insufficient production of spermatozoa or anomalies in the quality o spermatozoa products. Previous studies showed a correlation between Insulin resistance (IR) and reduced male fertility potential. The link between these diseases is probably the inflammatory backgroun associated with adipose tissue, particularly the visceral one, which is Insulin dependent. IR contribute significantly to availability of sex steroids through the production of sex hormone binding globulin (SHBG).

### Objectives

The aim of this study was to report a successful increase in the number and vitality of spermatozoa Insulin resistant and overweight patient who underwent only 6 weeks of very low calorie, carbohydrat free, protein based diet.

### Methods

In this study we report a case report of a 39-year old man with infertility due to oligoasthenospermia. Th patient was overweight (BMI 28), with waist circumference of 102 cm,with Insulin Resistance (HOMA 3,5 and liver fat. The man underwent 6 weeks of carbohydrate-free (ketogenic), protein based and strong hypocaloric nutrition therapy supplemented with Arginine, Maca and Ashwagandha. Ketone bodie Arginine, Lepidium meyenii (Maca) and Ashwagandha could support motility and vitality of spermatozoa ( 4).The number and quality of spermatozoa in semen analysis, the HOMA-IR (homeostasis mod assessment-estimated insulin resistance) index and the SHBG value is misured at To and T42.

### Results

Through rapid and consistent weight loss and improvement in insulin resistance, the very low calori ketogenic diet (VLCKD) and the supplements used produced an increase in sperm (from 5 million/ml to 1 million/ml) after only 6 weeks of carbohydrate-free diet. In relation to the sperm motility, the seme examination certified at To 5% of sperm with progressive movement, 5% with non-progressive movemer and 90% of spermatozoa are motionless. At T42 the spermatozoa with progressive movement represente 15%, 23% with non-progressive movement and 62% were motionless. For To morphological examination, 2 of normal spermatozoa and 98% of atypical forms were recorded, while T42 normal forms were 14% and th pathological 86%. VLCKD was associated with a significant increase in SHBG concentrations.

### Conclusions

The Ketogenic Diet supplemented with Arginine, Maca and Ashwagandha rapidly improved the sexu function, and reduced infertility in the overweight and insulin resistant man.

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