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DIETARY LIPIDSINTERFERING DRUG ABSORPTION: A DATA-BASED MINI-REVIEW

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Abstract

In bio-pharmaceutical viewpoint, absorption of drugs and their subsequent actions are influenced by various factors, including dietary components. In this paper, we have discussed the influence of dietary lipids on the absorption of drugs (mainly orally administered drugs) on the basis of database-based scientific reports. For this, we did a search in the PubMed, MedLine, ScienceDirect, and GoogleScholar databases for the up-to-date published evidences. Findings suggest that through several mechanisms dietary lipids affect in the pharmacokinetics of drug absorption processes. The absorption of fat soluble vitamins, and their analogues are dependent on the solubilisation of the drug in bile salt. Lipophilic drugs absorb better than the hydrophilic drugs with the dietary lipids. Some drugs are more absorbed with high fatty meals, while some are with medium or low and even no fatty meals .Here we mainly show the mechanism of drug absorption that interfere by the dietary lipids.

Keywords: *dietary lipids; drug absorption; pharmacological action*

Introduction

Drug absorption is the first step of the pharmacokinetic drug action, and is influenced by various factors, these include- co-administration of different kinds of foods, route of administration, disintegration and dissolution time, physico-chemical nature of drugs and the hosts' absorption site, and so on (B Shekhawat and B Pokharkar, 2017). Lipids are a part of our everyday meal that interfere drug absorption through different ways (Rezhdo et al., 2016). Lipophilic drugs are generally more absorbed with the fatty meals, while the hydrophilic drugs are impaired to absorb with the fatty meals (Porat and Dahan, 2018).

On the other hand, absorption of the drug is also influenced by the amount of dietary lipids present in the gastrointestinal tract (GIT). In some casesthe high amount of fatty diets increases the drug absorption more rapidly rather than the low amount of dietary fats (Amadi and Mgbahurike, 2018). On the other hand, sometimes low amount of dietary fats influenced drug absorption more than the high amount of dietary fats and also some drugs are absorbed more rapidly in the midium levels of fatty meal (Jeanes et al., 2004). In a sentence, dietary fats influence the absorption, thus the pharmacological action of drugs.

This paper aims to discuss the influence of dietary lipids on the absorption of orally administered drugs on the basis of an up-to-date databese reports.

Methods

We made a search with the keywords: 'dietary lipids' or 'dietary fats' paired with the 'interfering the absorption of drugs' in the following database: PubMed, MedLine, ScienceDirect, and GoogleScholar. Published evidences till Jun 2019 have been considered in this paper.

Findings

It has been seen that triglycerides and cholesterol are essential for the absorption and biological actions of many drugs (Ros, 2000).Co-administration of some drugs with the dietary lipids is evident to enhancethe absorption and therefore the bioavailability of those drugs (Zgair et al. 2016). Lipophilic drugs are better absorbed by the body than the hydrophilic drugs, it is due tothe physiological absorption site mainly composed of lipid permeable membranes (Murakami, 2017).

Mechanisms of dietary fats interfering drug absorption

Complex organic materials and triacylglycerols (>90% of the whole dietary fat), waxes, sterols, hydrocarbons, phospholipids and such kind of lipid substances are consist of dietary lipids (Goodman, 2010). The ingestion of dietary lipids increases solubility by the formation of an oil or emulsion phase, thus lipid soluble drugs absorption increases. Some physiological and biochemical reactions are initiated by the fatty meals that affect drug absorption through the secretion of bile and various lipases, gastric fluids; enzymatic hydrolysis of esterified lipids and emulsification, and solubilization of lipolytic products within the bile salt (Castro, 1991).

Hormone secretion from the GIT, lower gastric pH, high stomach emptying time and reduced gastrointestinal transit rates through a systematic mechanism (Weisbrodt, 1991). Rate of gastric emptying time (GET) was found to relate to the density of nutrients present in the meal; that's triacylglycerol and isocaloric concentration of carbohydrate show equal slowing of GET (Hunt and Stubbs, 1975). The stability of the emulsion phase within the gastrointestinal lumen prolong by the increased bile salt that enhances by the fatty meal (Friedman and Nylund, 1980). Constrained proof proposes that dietary fats do not change hepatic blood stream rather than protein initiated increment in splanchnic and hepatic blood streams (Orrego et al., 1965).

Various lipid soluble particles may end up joined into mixed micelles and transported into chylomicra by the epithelium before being discharged into the lymphatic flow (Wang et al., 2015; Markovic et al., 2019). Drug absorption by the lymphatic route appears to be only little importance for some highly lipophilic drugs (much more soluble in the chylomicra than in the plasma).Ordinarily, with the lipid enriched meal hydrophilic drug absorption is not significantly changed.

Fat-soluble vitamins and their analogs

Fat soluble vitamins (e.g., A, D, E and K)and their analogssuch as B-carotene, retinoids etcare

super lipid soluble. Intestinal absorption of fat soluble vitamins, and theiranalogs are dependent on the solubulization within the bile salt and form in exocytosed chylomicra in the enterocyte. Across the lymphatics and thoracic duct into blood the chylomicra are then expel [Castro GA (1991) 'Digestion and absorption. In Johnson LR,ed. Gastrointestinal physiology'. St Louis:Mosby,108-30.2,Barrowman JA. Intestinal absorption of the fat-soluble vitamins: physiology and pharmacology. In: C&y TZ, ed. Pharmacology of intestinal permeation II. Berlin: Springer-Verlag, 1984;647-89.

]. Radio-labeled fat-soluble vitamin in chylomicra was seen to absorb by the lymphatic route (Traber et al., 1988). Vitamins and vitamin analogs absorption is increased by the dietary fat intake. In a study, a un-changed in the concentration of serum B-carotene by the single 51 mg B-carotene dose was seen in the absence of dietary fat (Retzlaff et al., 1991). However, 50 mg of fats with this increased the serum concentration of the B-carotene. Isotretinoin, etretinate,acitretin are orally active retinoids increased bioavailability with fatty meals (Fleckman, 2003; Digiovanna et al., 2013). The enormity of the increase of absorption varies with different stage as like from medium to high increase of fat meal, absorption of retinoids does not enhance for the higher value (Colburn et al., 1983).

Cyclosporine

Cyclosporine mainly absorbed by the small intestines. This highly lipophilic and high molecular weight (1203 daltons) substance is an immunosuppressant agent also show the high binding affinity to lipoprotein (Wang et al., 2008). Cyclosporine with a high fat meal increased the AUC (Area Under the Plasma Concentration Time Curve) rather than the concurrent administration of low fat meal (Honcharik, 1991). Bile flow, which enhances the dietary fat consumption that act as the factor of solubility improvement, also promotes the absorption of cyclosporine, healthy people are not out of this process. For absorption of cyclosporine bile consist with the lymphatic route (Gupta et al., 1990).

Griseofulvin

Orally administered, anti-infective, low water soluble griseofulvin is absorbed, about 70 and 120% rapidly after administered with the 29.3 and 52.4% fatty food, respectively rather than in fasting stage (Ogunbona et al., 1985). It is due to the bile salt and lipid perfusion does not influence the duodenojejunal absorption of griseofulvin rate per area of the intestine (Palma et al., 1986). The high carbohydrate and protein meal without fat don't affect the absorption of griseofulvin (Crounse, 1961).

Atovaquone

Atovaquone, a highly lipophilic, water insoluble, anti-malarial and anti-protozoal compound that showed high absorption phenomenon when it was taken with the medium-fatty meal (28 gm butter on toast) to a high fatty meal (56 gm butter on toast) and increased AUC value 3 to 3.9 fold rather than the fasting state (Na-Bangchang et al., 2005). Improving drug solubility by the bile release and micelles formation is mainly happening for the fats that taken before 45 minutes of drug ingestion and hence drug absorption is increased (Zhi et al., 1995).

Halofantrine

Halofantrine, apoorly water soluble anti-malarial drug absorbed from the GIT, and is influenced by the fatty foods rather than the fasting condition. The value of AUC of this drug is increased 3 to 10 folds with highly fatty foods compared with the fasting stage (Milton et al., 1989).

Poorly formulated products

Mefenamic acid is a non-steroidal anti-inflammatory drug (NSAID) and anthranilic acid derivatives have low aqueous solubility and poor bioavailability and also the low dissolution rate (*in vitro*). A medium fatty meal increases the absorption of mefenamic acid. The formulation of mefenamic acid showedan improved bioavailability with an unaffected absorption in the presence of fatty food during the fasting periodof the host (Hamaguchi et al., 1986).

Phenytoin also shows the same phenomena; it did not affectby the amount of fat levels in the diet. In contrary, it was seen to improve its dissolution characteristicsin the biological fluids (Sekikawa et al., 1980). Medium fatty or highly fatty foods, mainly increase the absorption rather than

the fasting period, sometimes by increasing bioavailability and dissolution (Rezhdo et al., 2016).

Triglyceride-rich lipoproteins (TRL) absorption

Triglyceride-rich lipoproteins with the lipophilic compounds showed a significant pharmacokinetics absorption phenomenon. These are mainly absorbed by the lymphatic route. Fatty molecules of food, mainly bind with the TRLand decrease the volume of distribution and clearance, thus effect on the absorption of the drugs (Gershkovich and Hoffman, 2007).

Fattymeal on the pharmacokinetics of posaconazole

Posaconazole is an anti-fungal drug that absorbed within 3 to 5 hours. Posaconazole with the high or low fatty meal, absorption exceeds 90% and that is four times high rather than the fasting condition (Downer-Riley and Jackson, 2016).

Bronchiodilators and antitubercular drugs

Theophyllinealbuterol, and epinephrine are bronchodilators that are also evident to absorb better in the presence of dietary fatty food intake. Theophylline absorption by the body is increased with the presence of dietary fatty foods, while carbohydrate-rich meal decreases its absorption (Størmer et al., 1993). High fat meals decrease the concentration of serum cycloserine, an anti-tubecular drug (Zhu et al., 2001).

Conclusion

The absorption of many drugs is influenced by the dietary fatty foods. Generally dietary fats increase the absorption of lipophilic drugs and decrease the absorption of hydrophilic drugs. Therefore, it is important to maintain the amount of fats in our meal while taking these kinds of drugs as the amount of lipids ingested influence the absorption and pharmacological actions of the drugs. We also need to be careful about taking drugs, considering the foods' GET values.

Conflict of interest

None declared.

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