

## REVIEW ON MEDICINAL POTENTIAL OF ALKALOIDS AND SAPONINS

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### Abstract

Natural products are continuing to prove as a vital source of medicinally useful drug lead molecules. Although synthetic organic chemistry has achieved several milestones in human health improvement, due to several biological disadvantages, all synthetic chemistry are now using natural products as lead molecules / skeletal base for drug development. Among the medicinally significant natural products, alkaloids and saponins are known for their unique medicinal properties. The alkaloid is well known for its antibiotic and therapeutic applications, as many of the market available drugs and compounds are alkaloidal in nature. Saponins are generally known for its toxic property, with recent evidence of therapeutic possibilities, opening a new path for the medicinal research. This review focuses on the nature and potential of alkaloids and saponins as medicinally valuable compounds and summarizes some of the recent reports that describe the significance of the same. Although several works are being carried out on medicinal plants and beneficial microbes to identify their bioactivity and constituents, the majority of the pharmaceutical research is still at the crude extract stage, due to two reasons; complexity in purification of individual component due to quantity or quality, or due to symbiotic activity exhibited by more than one component in the same source. Hence, most of the scientific publications on pharmaceutical research, are still at the preliminary phase in the generalized activity of a plant or a microbe.

**Keywords:** *Natural products; alkaloids; saponins; medicinal properties.*

## Introduction

### Alkaloids

Alkaloids are probably the most bioactive phytochemical of all, with the potential to control gene expression, protein inhibition, and biochemical reactant. The key significant feature of alkaloid is the presence of nitrogen 'N' atom in its skeleton structure. An appropriate description of alkaloid is 'heterocyclic structure, consisting of a nitrogen atom within the ring structure'. Figure.1 shows the skeleton structure of caffeine - a classic alkaloid molecule. Presence of two or more types of cyclic hydrocarbon structure, i.e., 5 carbon, 6 carbon, or 7 carbon ring structure, with the presence of 'N' nitrogen atom within the cyclic skeleton makes it an alkaloid. Although alkaloids are majorly derived from amino acid metabolism, other sources also contribute to the synthesis and metabolism of alkaloids. Alkaloids are divided into three categories such as true alkaloids, protoalkaloids, and pseudoalkaloids. The compound which derived from amino acid and consist of a heterocyclic ring structure with nitrogen atom represent true alkaloids. The compound with N atom obtained from an amino acid represents protoalkaloids. The compound with the basic carbon skeletons which is not derived from amino acids represents pseudoalkaloids [1]. Alkaloids have the ability to act as a drug for anticancer, antimalarial and they include chemical compounds such as sulphur (S), oxygen (O), phosphate (P), and chlorine (Cl) [2]. Most of the alkaloids accommodate dihydropyrimidine which is backbones of calcium channel and they are secluded from sources like batzelladine alkaloids that are addressed to be effective HIV-gp-120-CD4 inhibitors [3].

Alkaloids serve as a hefty and structurally diversified group of secondary metabolites. They are structurally more analogous to some plant growth hormones. The existence of nitrogen in atomic construction consults that biological activity for this compound is tremendous [4]. Alkaloids play a substantial role in the metabolism and functional activities of an organism. Alkaloids are able to modify gene expression, due to their ability to bind and/or chelate with DNA. Alkaloids are physiologically effective in mammals, including

humans. Natural and synthetic alkaloids also known to function as narcotics. Alkaloids contribute as the main bioactive component of medicinal plant and also plays a very crucial role in the immune systems of animals and plants [5]. In traditional Chinese medicine, alkaloids were used as active compounds which have divergent biological activities. An extensive number of innate alkaloids may be molecular complexes derived from nucleic acid structures [6]. Because of their structural foible, alkaloids have relatively higher bioactive potential than the other classes of phytochemicals.

In addition to alkaloids derived from plants and microbes from terrestrial ambiance, the recent trend has taken attention on the marine source derived alkaloids. Marine alkaloids were initially identified from *Agelas* sponges and their synthetic analogs retain amply studied as inhibitors of bacterial biofilm formation and as antibacterial, antifungal and antiprotozoal agents [7]. Hundreds of secondary metabolites have been reported from marine sponges, with predominant chemical compounds exclusively belonging to the pyrrole-imidazole alkaloids family. This pyrrole-imidazole alkaloid is an extended family of metabolites exclusively found in marine sponges and are highly bioactive in nature [8]. Marine alkaloids are undoubtedly noble secondary metabolites, aiding to their novelty and complexity in structure and biological activity. Many marine alkaloids have entered and experienced several phases of human clinical trials for therapeutic use against particular types of cancers. Bryostatins, eribulin, plitidepsin, and trabectedin these are the compounds used in various phases of clinical trials [9].

A frequent biosynthetic origin of alkaloid is the tyrosine mediated pathway initially identified from divergent plant metabolites known as benzyloisoquinoline alkaloids. Due to their heightened potential in pharmacological activities, and natural accumulation in plants that are used in traditional medicine and cultural practices [10]. *Fusarium proliferatum* convert manzamine alkaloids to irrelevant manzamine metabolites via hydrolysis, reduction, and a retro Pictet-Spengler reaction. The propagation of tetrahydro- $\beta$ -carboline and tetrahydroisoquinoline ring systems is mainly by the Pictet-Spengler reaction. In the

biosynthesis of alkaloids, this reaction mainly involved from tryptophan including, the manzamine alkaloids [11]. Biological studies demonstrate apoptosis-inducing potential of *Tribulus terrestris* alkaloid extract on Jurkat E6-1 cancer cell line. At a sub-lethal concentration of alkaloids extract treated in Jurkat cells exhibit DNA fragmentation, augmentation in caspase-3 activity and phosphatidylserine translocation correlated to control cells [12].

### Natural Sources of Alkaloids

Plants serve as a major source of bioactive alkaloids, while still unparallel series of bioactive alkaloids have been reported from microbial sources as well. Recent evidence also proves that alkaloids could also be extracted from the animal kingdom. The plants are believed to be an effective source of alkaloids in comparison to the animal kingdom [13]. Alkaloids are an essential part of the biological metabolism. Hence, the source of alkaloids could be majorly generalized to all plants and microbial organisms, with countless reports in scientific studies. Some recent evidence of biological sources of alkaloids is summarized as follows. The most prevalent biologically active compound alkaloid is found within the Solanaceae family. The Solanaceae family is a widespread species which are rich in alkaloid content, with reported presence of tropane alkaloids, glycoalkaloids, pyrrolizidine and indole alkaloids that are naturally produced as a defense mechanism against insects and predators. The tropane alkaloids contain pharmacologically valuable properties but can also be noxious [14].

A rich source of alkaloids is found in marine sponges genus such as *Latrunculia*, *Batzella*, *Prianos*, and *Zyzyare*, majorly constructed on pyrroloiminoquinone ring system [9]. Naturally materializing indole alkaloids such as beta-carbolines, are found in plants and animal tissues. These alkaloids are distinguished by a core indole structure combined with a pyridine ring. Alkaloids are extensive in our environment, diets and can also be composed endogenously that are initially recognized from the plant sources, e.g. *Peganum harmala* [15]. Natural compounds from marine organisms such as neurosteroidal alkaloid isolated from jellyfish act as an effective anti-AChE agent

with strong inhibition potential, by binding to the catalytic site of acetylcholinesterase [16]. Endophytic fungi act as dominant resources for structurally particular bioactive metabolites such as alkaloids, benzopyranones, benzoquinones, flavonoids, phenols, steroids, and xanthenes [17]. These endophytic fungi have proven to serve as a source for several pharmaceutical applications.

*Lycium shawii* and *Phyllanthus emblica* seeds hold an enormous amount of active phytochemicals like alkaloids, phenolic compounds, tannins, and flavonoids, with key studies focusing on alkaloids of this seeds [18]. Several alkaloids were identified in flowers of *Tecomella undulate* that are biologically efficient alkaloids [2]. Rich sources of natural bioactive compounds alkaloids are found in herbal based beverages such as tea, wine, beer, etc., [19]. Some of the important bioactive compounds present in herbal teas include carotenoids, phenolic acids, flavonoids, coumarins, alkaloids, polyacetylenes, saponins, and terpenoids.

### Saponins

Saponins are complex phytochemical molecules, consisting of two key moieties. A lipophilic sapogenin moiety and a hydrophilic sugar moiety, combination of which contribute to the characteristic soapy / detergent nature of Saponins. The structural description of saponin would be 'Combination of a lipophilic sapogenin moiety with one or more hydrophilic sugar moiety'. Originally saponins are identified and studied from plants, with recent reports on occurrences in other natural sources. Figure.2 provides a description of the skeleton structure of a saponin, with Chonglou saponin as an example.

Saponins are a complex combination of triterpene glycosides with a broad spectrum of biological properties such as antifungal, insecticidal, phytotoxic, allelopathic, and hemolytic activity [20].

A divergent group of biologically functional products in the plant are triterpene saponin, which exhibits broad structural variety. Saponins are responsible for the tenacious astringency tastes of soybean. DDMP (2, 3- dihydro-2,5-dihydroxy-6-methyl-4H-pyran-4-one) saponins have been proven to control dietary hypercholesterolemia,

suppression of colon cancer cell proliferation, antiperoxidation of lipids and liver-protecting action by the acceleration of secretion of thyroid hormones.[21] *Paris polyphylla* root is a natural product that shows admirable and decent sources for the pharmaceutical development of anticancer drugs. Saponins of different herbs are known to induce apoptosis in many cancer cells. Paris saponin VII a kind of steroidal saponins from the root of *P. polyphylla*, on the human cervical cancer cell line Hela and the potential for the treatment of cervical cancer [22]. The saponin fraction isolated from the roots of *Gypsophila paniculata* L. and *Gypsophila arrost* Guss represented as Merck Saponin and digitonin was used to scrutinize our knowledge of the interaction among amphiphilic glycosides and cell membranes. These saponins include structural motifs that are similar to membrane sterols and exhibit a higher affinity for cholesterol compared to phosphatidylglycerols [23].

### Natural Sources of Saponins

Plants and algae are the major sources of Saponin, with rare reports from microbial sources. Affluent sources of saponins are found in an array of plant species such as *Chlorophytum borivilianum*, *Glycyrrhiza glabra*, *Panax ginseng*, *Bacopa monnieri* and, *Ilex paraguariensis*. These plants possess immunomodulatory, antidiabetic, gesticulatory, antimicrobial, insecticidal, and androgenic activities primarily associated with the immense quantity of saponins present in the plants [24]. A wide diversity of saponins are reported from plants such as *Yucca schidigera*, *Quillaja Saponaria*, *Acacia auriculiformis*, *Sapindus saponaria*, *Sesbania sesban*, and *Medicago sativa* [25]. The leguminous plant of *Lessertia frutescent* showed the presence of saponins cardiac glycosides. Saponins are present in high quantity in the aerial parts of such leguminous plant [26].

Some of the recent reports of Saponin based bioactivities are as follows; *Phaleria macrocarpa* is used as traditional medicine in Indonesia for medical conditions such as cancer, diabetes mellitus, allergies, liver and heart diseases, kidney failure, blood diseases, high blood pressure, stroke, various skin diseases, itching, aches, and flu. The hefty amount of saponin glycosides

existing in *P. macrocarpa* can devote to the plant's bioactivities such as anti-oxidant and cytotoxicity [27]. *Pteropyrum scoparium* is a medicinally essential plant and it is used to cure dyspepsia and blood purifying agent. The several bioactive compounds found in this plant such as anthraquinones, and Saponins [28].

*Panax ginseng* of Araliaceae family is a perennial herbaceous plant which contains polyacetylenes, polysaccharides, peptidoglycans, phenolic compounds, and saponins. Isopentenyl diphosphate can be synthesized through the mevalonate pathway in the cytosol and it is a universal precursor for Triterpene saponins, including ginsenosides [29]. *Azadirachta indica* belongs to the Meliaceae family and that contains biologically important alkaloids and saponins. Due to its unparallel pharmacological activities, it is one of the most valued medicinal plant in India [30].

Among the significant traditional Chinese herbs, *Astragalus membranaceus* Bge. var. *mongolicus* of Leguminosae family is well known for its high bioactivity. It produces diverse secondary metabolites such as triterpene saponins. The genes in MVA and non-MVA pathways were differentially articulate among three tested tissues, indicating the parallel but fractionally divided biosynthesis pathways of IPP and DMAPP in *A. mongolicus* in triterpene saponin biosynthesis [31]. The *Panax notoginseng* plant of Araliaceae family is a pharmaceutically essential plant which contains a significant amount of triterpene saponins. The transcripts encrypt the critical enzymes of Acetyl-CoA acetyltransferase, squalene epoxidase and dammarenediol synthase in this plant play imperative roles in triterpene saponin biosynthesis [32].

*Barbarea vulgaris* is a wild crucifer of the Brassicaceae family and it is only species which is cost-effective and are able to produce saponins. These saponins play a role in defense against biotic antagonists. Monoglucosylated 3-O- $\beta$ -D-Glc hederagenin, produced in vitro by glycosyltransferases functions contrary to *Phyllotreta nemorum* professed 3-O-glucosylation Saponin, suggesting variation in activity through the mode of synthesis [33]. In *Medicago truncatula*, saponin is the essential biologically active secondary metabolite [20].

### Anti-Bacterial Activity of Alkaloids

The antibacterial activity being the most prevalently studied biological activity, a countless number of scientific reports are available proving the antibacterial nature of alkaloids compounds, of both natural and synthetic origins. Some of the recent reports on antibacterial activities of alkaloids are summarized in Table.1, that are discussed in this review.

*Allium sativum*, *Bunium persicum*, *Oryza sativa*, and *Triticum aestivum* are traditionally used antimastitis plants shows antibacterial activity against *Escherichia coli*, *Klebsiella pneumoniae*, and *Staphylococcus aureus*. Alkaloids of *Allium sativum*, *Bunium persicum*, *Oryza sativa*, and *Triticum aestivum* showed strong bacterial inhibition zones as compared to crude Flavonoid and Saponin extract [34]. *Inula cuspidate* is used as folk medicines like a tonic, stomachic, anti-inflammatory, bactericidal, diuretic, diaphoretic, hepatoprotective, antitumor and carminative. Due to the presence of a rich source of alkaloid based secondary metabolites, the plant extracts show significant antibacterial activity [35]. The antibacterial activity of plants such as *Curcuma xanthorrhiza*, *Ocimum sanctum*, *Senna alata*, *Kaempferia pandurata*, *Zingiber officinale*, *Moringa oleifera*, *Tamarindus indica*, and *Pangium edule* studied against methicillin-resistant *Staphylococcus aureus*. These plants consist significant amount of alkaloids, among which *Senna alata* leaf extract exhibits the highest significance of activity [36]. The *Calophyllum tomentosum* extract consists of alkaloids, that are believed to be responsible for the inhibition of  $\alpha$ -glucosidase activity, anti-bacterial, anti-oxidant, anti-diabetic, anti-inflammatory and anti-tyrosinase activity [37].

Antibacterial secondary metabolite alkaloids such as Marinoazepinone A, Marinoazepinone B, Marinoaziridine A, Marinoaziridine A, Marinoquinoline G, Marinoquinoline H, Marinoquinoline I, Marinopyrazinone A, Marinopyrazinone B, Marinoquinoline A, Marinoquinoline C, Marinoquinoline D, Marinoquinoline K and Marinoquinoline were isolated from two strains of marine bacteria *M. alkaloidigena* and *C. alkaloidigena* [38].

*Gracilaria verrucosa* seaweed is an effective antibacterial source containing an alkaloid, compounds. This seaweed showed antibacterial activity against *Aeromonas hydrophila*, *Pseudomonas aeruginosa*, *Pseudomonas putida* and had weak antibacterial activity against *Vibrio harveyi* and *Vibrio alginolyticus* bacteria.[39] *Enterolobium contortisiliquum* is a seed bark to estimate its antibacterial activity and is a potent antibiotic against strains of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Escherichia coli*. [40] *Aconiti Lateralis* containing alkaloids was used in traditional Chinese medicine for treatment of *Escherichia coli* and *Staphylococcus aureus*. In *Staphylococcus aureus*, there is a signifying reluctant growth and metabolism by the *Aconitum* alkaloid treatment [41].

*Cienfuegosia digitata* Cav. is an herbal medicinal plant used as traditional medicine in Burkina Faso. This plant is rich in saponins and alkaloids compounds with strong potential as a broad-spectrum antimicrobial agent. The alkaloids compounds present in this plant have the antibacterial activity against  $\beta$ -lactamase producing Methicillin and Ampicillin-resistants *Staphylococcus aureus* (MRSA / ARSA) [42]. Several alkaloids were identified from marine organisms such as marine invertebrates, microbes, fishes and microalgae. These alkaloids consist of both alkaloid secondary metabolite and small peptide molecules, with strong anti-bacterial activity against drug-sensitive and drug-resistant pathogens [43].

The stem bark and root extracts of *Thalictrum rhyncocarpum* contain glycosides and alkaloids with antibacterial activity against *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Mycobacterium vaccae*. The plant *T. orientale* exhibited antimicrobial activity against *Staphylococcus aureus*, *Salmonella gallinarum*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, and *Candida albicans*. This antibacterial activity is claimed to be due to the large number of alkaloids present in *T. rhyncocarpum*. Additionally *T. rhyncocarpum*, has been used extensively in traditional medicine to treat stomach ulcers, snake bites, dysentery, and skin rashes due to the presence of bioactive alkaloids [44]. *Evodia rutaecarpa* is a bitter herb

used in traditional Chinese medicine, proven to contain limonoids and alkaloids with antibacterial activities against *E.coli* and *S.aureus*. The antibacterial examination suggested limonoids had greater antibacterial properties than alkaloids, and that indoloquinazoline alkaloids had greater antibacterial activities than quinolone alkaloids [45].

Marine sponges are the rich source of bioactive compounds with divergent function. They are claimed to be the sources of the non-traditional anti-bacterial agent. Pyrrole-imidazole alkaloids produced by these marine sponges are proven to inhibit biofilm formation and suppress antibiotic resistance against the Gram-negative *Acinetobacter baumannii* and Gram-positive methicillin-resistant *S.aureus*. It is strongly believed that marine sponges derived alkaloids may probably serve as an eminently useful source of scaffolds for non-traditional anti-bacterial access [46]. These marine alkaloids could lead to the development of novel antibacterial drugs in the future.

### Anti-Parasitic Activity of Alkaloids

Parasitic diseases are majorly caused in human as well as an animal which cause a significant fiscal loss. Protozoan induced diseases being one of the major health problem faced by Asian countries, these anti-parasitic studies are quite common in India and China. Alkaloids have proven their effectiveness as a significant anti-parasitic agent in several clinically important parasitic diseases. Some of the recent reports on this are summarized in Table.2 that is discussed in this review.

The antiparasitic plants of the *Asteraceae* family are proven to be effective in the treatment of parasites and that it can inhibit the progression of protozoan parasites such as Plasmodium, Trypanosoma, Leishmania, and intestinal worms. *Asteraceae* is recognized for its alkaloid content. Some of the FDA-approved nature-derived drugs that emanate from *Asteraceae* as antiparasitics are; Arteether, Artemether, Artemisinin, Artesunate, Coarsucam, Co-Artemether, Dihydroartemisinin, And Santonin [53].

Praziquantel is a drug which is used to cure the parasitic infection schistosomiasis. In the developmental assay, ergot alkaloids are able to

modulate the schistosomules. Ergot alkaloids have been used clinically in a range of treatment such as a migraine, obstetrics, Parkinson's disease, and diabetes [54]. A divergent group of the compound in ergot alkaloids with beneficial therapeutic effect used as anthelmintic drug design that integrates deleterious antiparasitic activity. Ergotamine declined fatality, parasite load, and intestinal egg counts but the organ pathology also abates through engagement of host G protein-coupled receptor that suppressed hepatic stellate cell activation, inflammatory damage, and fibrosis. Ergotamine drug is used to treat migraines, strongly interacted with the target protein. Ergotamine is used to treat infected mice that eliminated the parasites and decrease the organ damage induced by the infection [55].

The traditional Mexican medicinal plant *Laennecia confusa* and *Asteraceae* has potential benefit as antibacterial, antifungal, anti-inflammatory, and antiparasitic agent [56]. These plants proved to contain bioactive alkaloids, that contributes towards the reported activities. *Pelliciera rhizophorae* is a potential antiparasitic anti protozoan with high selectivity to the parasite and low cytotoxicity to the host [57]. Single-celled parasites disease like malaria, leishmaniasis, and Chagas disease were reported to be treated by Colombian sponges *Verongula rigida*, that also claims to contain antimicrobial, anti-enzymatic, cytotoxic and antiparasitic activities [58]. Didemnidines and two indole spermidine alkaloids were isolated from the *Didemnum* sp. Didemnidine exhibit moderate antiparasitic activity against the malaria parasite *Plasmodium falciparum* [4].

A potent antiinfective and antiparasitic 2, 3-dihydro-1H-indolizinium chloride were isolated from *Prosopis glandulosa* Torr. var. *glandulosa*. Ethanol extract of *Prosopis glandulosa* Torr. var. *glandulosa* showed less in vitro antiinfective and antiparasitic activities [59]. Alkaloids from marine invertebrates shown powerful bioactivity in multiple antiparasitic screening studies, with the greatest potency against *T. brucei* and *P. falciparum* [60]. *Albizia schimperiana* Oliv is a tree which is used as an indigenous treatment for bacterial and parasitic infections, like malaria, pneumonia, pain relief and fever. The alkaloid portion in MeOH extract of *Albizia gummifera* stem

bark maintained significant activities such as antimicrobial, antiparasitic, antitrypanosomal, and mosquito larvicidal [61].

### Anti-Diabetic Activity of Alkaloids

Diabetes mellitus is a combination of metabolic disorders distinguished by the existence of a chronic hyperglycemia due to defective insulin or insulin secretion [66]. Medicinal plants play a major role in the management of diabetes mellitus [67]. The leaves of *Cayulsea abyssinica* contains glycosides, alkaloids, terpenoids, flavonoids, polysaccharides, and saponins, which are repeatedly involved in having an anti-diabetic effect. *C. abyssinica* shows a significant antidiabetic effect in rodents, providing evidence for the Ethiopian folklore medicine. Alkaloids are claimed to be significant for this observed antidiabetic activity [66].

*Aegle marmelos* (L.) Corr. is an Indian traditional medicine, is used to cure fevers, abdomen pain, palpitation of the heart, urinary troubles, melancholia, anorexia, dyspepsia, diabetes, and diarrhea [68]. The stem bark of *Aegle marmelos* Correa has antidiabetic, antihyperlipidemic and antioxidant activity. It is proven to contain umbelliferone  $\beta$ -D-galactopyranoside. The umbelliferone  $\beta$ -D-galactopyranoside possesses an antidiabetic, antioxidant and antihyperlipidemic effect on the streptozotocin-induced diabetic rat decreases elevated blood glucose in diabetic rats. The umbelliferone  $\beta$ -D-galactopyranoside treatment has increased the level of good cholesterol, triglycerides, VLDL, LDL cholesterol and decreased the level of HDL cholesterol and liver Malondialdehyde [68].

*Catharanthus roseus* is an Ayurvedic medication used in countries like India, South Africa, China and Malaysia for the healing of diabetes mellitus. Ethanol extract of *C. roseus* has proven to exhibit a significant anti hyperglycemic activity in STZ-induced diabetic rats. Roots and leaves of this plant contain more than 100 alkaloids. The significantly important group of alkaloids from this plants are identified as vinblastine and vincristine [69]. The leaves and roots of *Uvaria chamae* exhibit a strong presence of alkaloids. The hydroethanolic root extract of *Uvaria chamae* has demonstrated

strong antidiabetic and hypolipidemic activities in streptozotocin-induced diabetic rats [70].

*Trigonella foenum-graecum* is a medicinal herb possesses diverse biological activities and pharmacological functions. It contains steroids and alkaloids that were traditionally used in the treatment of diabetes including high cholesterol, inflammation, and gastrointestinal ailments. Ethanol extract of *T. foenum-graecum* seed significantly decreased blood glucose level in alloxan-induced rats [71]. The ethanol extract of *Brucea javanica* seed contains alkaloids, polyphenols, and flavonoids. *B.javanica* seed extract demonstrated significant antidiabetic activity diabetes-induced rat models [72].

Plants belonging to families such as *Leguminosae*, *Lamiaceae*, *Liliaceae*, *Cucurbitaceae*, *Asteraceae*, *Moraceae*, *Rosaceae*, *Euphorbiaceae*, and *Araliaceae* have proven to contain antidiabetic activity. They contain alkaloids as their key bioactive ingredient. Peroxisome proliferator-activated receptors have the potential gamma partial analogs 12 molecules from these extracts known to have antidiabetic activity. So far Metformin is the only drug approved for treatment of type 2 diabetes mellitus derived from a medicinal plant [73].

### Anti-Bacterial Activity of Saponins

Saponins, in general, are reported to be significant antibacterial agents, and several plants are claimed to be antibacterial in nature, due to the presence of complex Saponins. Table.3 summarizes some of the recent reports on the antibacterial activity of saponins, discussed in this review.

An affluent source of saponins is present in an array of plant species such as *Colocasia esculenta*, *Triumfetta pentandra*, *Canarium schweinfurthii* and *Annona muricata* exhibit broad-spectrum antibacterial activity against *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, *Enterobacter aerogenes*, *Bacillus subtilis*, *Escherichia coli*, and *Providencia stuartii* [74].

*Sesbania grandiflora* is a tree belonging to Fabaceae family that contains a significant amount of bioactive saponins. The leaf extract of *S. grandiflora* display confirmation of high antibacterial activity and anti-biofilm property against

*S. aureus*. It is used as a traditional medicine to treat nasal catarrh, nyctalopia, and cephalagia. It is also recognized as an antioxidant, anti-arthritis, antiurothiatic, anti-inflammatory, anticonvulsive, anti-helminthic, and anxiolytic activity [75]. The antibacterial activity of plants such as *Anethum graveolens*, *Foeniculum vulgare* and *Trachyspermum ammi* belonging to the family Umbelliferae reported against *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Shigella flexneri* are claimed to be due to bioactive saponin content present in them [50].

The *Artemisia chamaemelifolia* of Asteraceae family is known for its ability to produce secondary metabolites such as Saponins and alkaloids. *A. chamaemelifolia* has been used as an antiparasitic, antifungal, antitumor, antihelminthic agent, it is also known as an antibacterial plant with activity against *Bacillus cereus*, *Salmonella typhimurium*, *Pseudomonas aeruginosa*, and *Listeria monocytogenes* [76]. *Commelina nudiflora* has potential in-vitro antioxidant and antimicrobial activity against *Pseudomonas aeruginosa* and *Escherichia coli*. This plant *C. nudiflora* is a perennial herb belonging to the Commelinaceae family consist of important bioactive clusters of Saponins and alkaloids contributing towards the observed activity [77].

The antibacterial activities of Cameroonian medicinal plants *Albizia adianthifolia*, *Alchornea laxiflora*, *Boerhavia diffusa*, *Combretum hispidum*, *Laportea ovalifolia* and *Scoparia dulcis* against multidrug-resistant Gram-negative bacterial strains such as *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Enterobacter aerogenes*, *Escherichia coli*, and *Providencia stuartii*. The most significant antibacterial activity among these plants was recorded with bark and root extracts of *A. adianthifolia* as well as with *L. ovalifolia*. These plants consist of a diverse group of saponins, contributing to the antibacterial activity [78]. *Cestrum nocturnum* belonging to the Solanaceae family has been used in the treatment of burn and swelling, as an analgesic and bactericidal, local anesthetic, cardiac arrhythmic, and for its inhibitory effect on the central nervous system, tumor inhibition, and antioxidant ability. The bactericidal activity of *Cestrum nocturnum* plant

was observed against *Citrobacter*, *Salmonella typhi*, *Enterococcus faecalis*, *Escherichia coli*, *Proteus vulgaris*, and *Vibrio cholera* is believed to be contributed due to the presence of saponins [79].

In the traditional Chinese medicine, *Callistemon viminalis* belonging to family Myrtaceae is known for its Saponin content is used for treating hemorrhoids and consists of antibacterial activity against *Bacillus cereus*, *Bacillus subtilis*, *Escherichia coli*, *Sarcina lutea*, *Pseudomonas aeruginosa*, and *Salmonella typhi* [80]. *Mentha piperita*, *Portulaca oleracea*, and *Raphanus sativus* these are a medicinal plant that contains antioxidant, antibacterial, anti-inflammatory, antiviral, immunostimulant and detoxification activities. These plants exhibit antibacterial activity *Staphylococcus aureus*, *Streptococcus pyogenes*, *Escherichia coli*, *Bacillus subtilis*, and *Pseudomonas aeruginosa* [81].

The liquid decoctions and the homogenized root of *Paullinia pinnata* are used in Nigeria, Togo and Ghana conventional medicine for treating inflammation, lesion, snake bites and more diseases like erectile dysfunction, malaria, dysentery, menstrual pain, and coughs. Due to the presence of alkaloid, triterpene saponins, and a glycoside, *P. pinnata* exhibit strong antibacterial activity against the *Escherichia coli*, *Bacillus subtilis*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Shigella dysenteriae*, and *Clostridium tetani*. [82].

### Anti-Parasitic Activity of Saponins

The Parasitic diseases such as malaria and leishmaniasis that affects a major public of the world global population. Saponins have proven to be a vital source in many anti-parasitic studies. Some of the literature discussed in this review are summarized in Table.4. Leishmaniasis is caused by protozoan *Leishmania* parasites which are transferred by sand flies. *Maesa balansae* methanolic extract were evaluated against drug-sensitive visceral *Leishmania* strains. *M. lanceolata*, *M. sinensis*, *M. crassifolia*, *M. tomentella*, and *M. balansae*. These plants show antileishmanial potential against *Leishmania donovani* and *Leishmania infantum* [83]. *Pelliciera rhizophorae* of Pellicieraceae family is a mangrove plant known as a good source of secondary metabolites such as



alkaloids, saponins, and other bioactive phytochemicals. *P.rhizophorae* demonstrates divergent medicinal uses such as to cure skin infections, tuberculosis, skin wounds, diarrhea, and parasites, including protozoa and helminthes. *P. rhizophorae* act as an antiparasitic agent against *Leishmania donovani*, *Tripanosoma cruzi*, and *Plasmodium falciparum* [57].

*Pittosporum mannii* is a Pittosporaceae family is a traditional medicinal plant to cure malaria and it has shown the presence of flavonoids and saponins. The methanol extract of *P. mannii* shows the antiparasitic activity against *Leishmania donovani* and *Plasmodium falciparum* [84]. *Laennecia confusa* is traditional Mexican medicinal plants the chloroformic extract have the antiparasitic activity for *Leishmania donovani*. The Asteraceae family possesses antimicrobial, antiparasitic, and anti-inflammatory bioactivities [56]. *Laennecia confusa* is a traditional Mexican medicinal plant, from which the chloroform extract have shown antiparasitic activity against *Leishmania donovani*. The Asteraceae family is well known to posses antimicrobial, antiparasitic, and anti-inflammatory bioactivities [53]. *Platycodon grandiflorum* is a plant exert a wide range of pharmacological activities, including anti-inflammatory, vasoprotective, hypocholesterolemic, immunomodulatory, hypoglycemic, molluscicidal, antifungal, and antiparasitic functions. *P. grandiflorum* contain triterpenoid saponins secondary metabolites of glycosidic nature [85].

### Anti-Diabetic Activity of Saponins

Diabetes mellitus is a metabolic disorder mostly accompanied by long-term complications and categorized into diabetes type 1 which is a result of insulin deficiency and diabetes type 2 is due to insulin resistance that affects a big part of the world's global population. *Caralluma Europaea* is a medicinal plant biological activity such as antinociceptive, anti-inflammatory hepatoprotective and potent antihyperglycemic properties. The aerial part of shrub juice is used to treat diabetes, goiter, and cyst, and it is known to contain bioactive saponins [67]. *Prosopis juliflora* is a medicinal plant used as veterinary medicine as well as antidiabetic, anti-inflammatory, anticancer,

and antimicrobial activities. This plant has major antidiabetic activity due to the presence of alkaloids and saponins. It contains 24-methylencycloartan-3-one which is proven to be safe to treat diabetes mellitus instead of using insulin [89].

*Derris reticulate* which is known to consist saponins demonstrates antihyperglycemic activity by the cytoprotective result on pancreatic cells and also demonstrates antioxidant activity, and inhibition of the enzyme  $\alpha$ -glucosidase [90]. *Semecarpus Anacardium* possesses strong anti-diabetic and antioxidant activity and used for the treatment of diabetes mellitus and a good source of natural antioxidants [91]. *Tapeinochilus ananassae*, *Costus speciosus*, and *Syzygium Jambos* are the plants with a rich source of Saponin. This plant exhibit hypoglycemic activity which is showed in insulin-like effects in streptozotocin-induced diabetic rats [92].

### Conclusion

Alkaloids and Saponins are undoubtedly a valuable source and are highly significant lead molecules for drug development. Alkaloids have influenced the medicinal research, where the majority of market available drugs are alkaloid molecules. Although not very significant, saponins are starting to play a key role in the medicinal field, by slowly proving their effectiveness and applicability in clinical research. This review paper concludes that alkaloid and saponins are definitely the most significant bioactive molecules in the plant secondary metabolites and still are in the path of research and exploitation to be fully employed in human health applications.

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**Table 1:** Reports on the antibacterial activity of alkaloids

Source	Compound	Activity	Reference
<i>Sida acuta</i>	Crude alkaloids	<i>Staphylococcus aureus</i> , <i>Enterococcus faecalis</i> , <i>Shigella boydii</i> , <i>Shigella flexneri</i> , <i>Shigella dysenteriae</i> , <i>Salmonella typhi</i> , <i>Salmonella paratyphi</i> , <i>Escherichia coli</i>	Damintoti karou et al., 2006 [48]
<i>Sophora alopecuroides</i>	Alkaloids	<i>Staphylococcus epidermidis</i>	Xue Li et al., 2006 [49]
<i>Sarcomelicope megistophylla</i>	Megistoquinones	<i>Escherichia coli</i> , <i>Staphylococcus aureus</i> , <i>Staphylococcus epidermidis</i> , <i>Pseudomonas aeruginosa</i> , <i>Enterobacter cloacae</i> , <i>Klebsiella pneumonia</i>	Nikolas fokialakis et al., 2002 [50]
<i>Anethum graveolens</i> , <i>Foeniculum vulgare</i>	Crude alkaloids	<i>Shigella flexneri</i>	Gurinder J Kaur et al., 2009 [51]
<i>Zizyphus oxyphylla</i>	Cyclopeptide Alkaloids	<i>Escherichia coli</i> <i>Bacillus subtilis</i> <i>Shigella flexeneri</i> <i>Staphylococcus aureus</i> <i>Pseudomonas aeruginosa</i> <i>Salmonella typhi</i>	Waqar Ahmad Kaleem et al., 2012 [52]
<i>Piper nigrum</i> , <i>Telfairia occidentalis</i> , <i>Vernonia amygdalina</i>	Crude alkaloids	<i>Escherichia coli</i> , <i>Pseudomonas aeruginosa</i> , <i>Enterobacter aerogenes</i> , <i>Enterobacter cloacae</i> , <i>Klebsiella pneumoniae</i> , <i>Providencia stuartii</i>	Victor Kuete et al., 2013 [53]



**Table 2:** Reports on the anti-parasitic activity of alkaloids

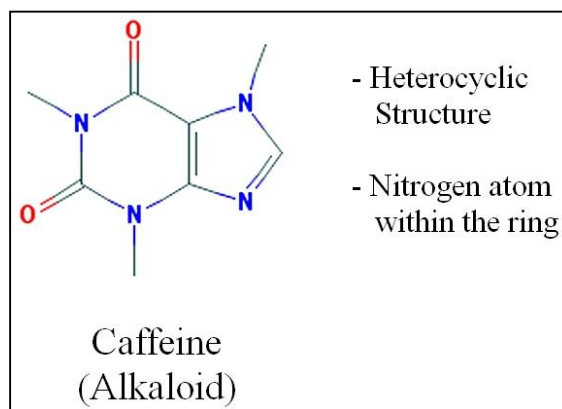
Source	compound	Activity	Reference
<i>Albizia schimperiana</i> Oliv.	Budmunchamines	<i>Leishmania donovani</i>	Volodymyr Samoylenko et al., 2009 [62]
<i>Annona coriacea</i> , <i>Annona crassiflora</i> , <i>Cissampelos ovalifolia</i> , <i>Duguetia furfuracea</i>	Isoquinoline alkaloids	<i>Leishmania (L.) chagasi</i>	A.G. Tempone et al., 2005 [62]
<i>Prosopis glandulosa</i> ;	indolizidine alkaloids	<i>Leishmania donovani</i>	Aziz Abdur Rahman et al., 2011 [63]
<i>Prosopis glandulosa</i> Torr. var. <i>glandulosa</i> .	Indolizidine	<i>Plasmodium falciparum</i>	Volodymyr Samoylenko et al., 2009 [59]
<i>Peganum harmala</i>	$\beta$ -carboline	<i>Leishmania donovani</i>	Rihui Cao et al., 2007 [64]
<i>Annona foetida</i>	pyrimidine- $\beta$ -carboline alkaloid	<i>Leishmania braziliensis</i> .	Emmanuel V. Costa et al., 2006 [65]

**Table 3:** Reports on antibacterial activity of saponins

Source	Compound	Activity	Reference
<i>Anethum graveolens</i> , <i>Foeniculum vulgare</i> , <i>Trachyspermum ammi</i>	Crude saponin	<i>Staphylococcus aureus</i> , <i>Pseudomonas aeruginosa</i> , <i>Salmonella typhimurium</i> , <i>Shigella flexneri</i>	Gurinder J Kaur et al., 2009 [50]
<i>Acacia auriculiformis</i> , <i>Calliandra tergemina</i> , <i>Peltophorum pterocarpum</i>	Crude saponin	<i>Micrococcus luteus</i> <i>Staphylococcus aureus</i> <i>Bacillus cereus</i>	Yik Ling Chew et al., 2011[86]
<i>Callistemon viminalis</i>	Crude saponin	<i>Bacillus cereus</i> , <i>Bacillus subtilis</i> , <i>Escherichia coli</i> , <i>Sarcina lutea</i> <i>Pseudomonas aeruginosa</i> , <i>Salmonella typhi</i> .	Mohamed ZM Salem et al., 2013 [80]
<i>Clausena heptaphylla</i>	Crude saponin	<i>Salmonella typhi</i> , <i>Klebsiella pneumoniae</i> , <i>Shigella flexneri</i> , <i>Shigella sonnei</i> , <i>Vibrio cholerae</i> , <i>Pseudomonas aeruginosa</i>	Md Fakruddin et al., 2012 [87]
<i>Sechium edule</i> , <i>Manihot esculinta</i>	Crude saponin	<i>Providencia stuartii</i> , <i>Pseudomonas aeruginosa</i> , <i>Klebsiella pneumoniae</i> , <i>Escherichia coli</i> , <i>Enterobacter aerogenes</i> <i>Enterobacter cloacae</i>	Jaurès AK Noumedem et al., 2013 [88]
<i>Artemisia chamaemelifolia</i>	Crude saponin	<i>Bacillus cereus</i> <i>Salmonella typhimurium</i> <i>Pseudomonas aeruginosa</i>	Ghasemi Pirbalouti et al., 2013 [76]
<i>Colocasia esculenta</i> , <i>Triumfetta pentandra</i> , <i>Canarium schweinfurthii</i> , <i>Annona muricata</i>	Crude saponin	<i>Pseudomonas aeruginosa</i> , <i>Klebsiella pneumoniae</i> , <i>Enterobacter aerogenes</i> , <i>Escherichia coli</i> , <i>Bacillus subtilis</i> , <i>Salmonella typhi</i>	Joachim K et al., 2016 [74]

**Table 4:** Reports on antiparasitic activity of saponins

Source	Compound	Activity	Reference
<i>Maesa balansae</i>	Triterpene Saponins	<i>Leishmania infantum</i> <i>Leishmania donovani</i>	Louis Maes et al., 2003 [83]
<i>Pittosporum mannii</i>	Triterpenoid Estersaponin	<i>Leishmania donovani</i> <i>Plasmodium falciparum</i>	Kennedy D Nyongbela et al.,2013 [84]
<i>Pelliciera rhizophorae</i>	Crude saponin	<i>Leishmania donovani</i> <i>Tripanosoma cruzi</i> , <i>Plasmodium</i> <i>falciparum</i> ,	Dioxelis López et al., 2015 [57]
<i>Laennecia confusa</i>	Crude saponin	<i>Leishmania donovani</i>	Mar'ia G.Mart'inez Ruiz et al., 2012[56]
<i>Eclipta prostrata</i>	Crude saponin	<i>Leishmania donovani</i>	Sujogya Kumar Panda et al., 2018 [53]

**Figure 1:** The skeleton structure of a classic alkaloid - caffeine**Figure 2:** The skeleton structure of saponin - Chonglou saponin