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SHORT REVIEW

# Exploring Recent Advancements in the Pharmacological Activities of Plant-derived Alkaloids and Glycosides: A Review

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## Abstract

A wide spectrum of bioactive compounds is synthesised by plants, and these agents act as protection systems against different living and non-living stressors. They are also useful in the manufacturing of pharmaceutical medications which alleviate a range of human illnesses. Numerous plant metabolites, including glycosides as well as alkaloids, have been studied for potential uses as antioxidants and medicinal agents. Numerous research assessed the modes of action of compounds, therapeutic and pharmacological uses and noteworthy health advantages (such as antifungal, anti-swelling, antimicrobial and anti-tumour applications). As such, a bid has been made to offer an overview of the most recent research that has been done into the secondary metabolites found in medicinal plants.

**Major Findings:** Recent advances in the pharmacological activity of plant-derived alkaloids and glycosides emphasize their expanded therapeutic potential through better drug delivery mechanisms and synergistic uses.

**Keywords:** Alkaloid, Glycoside, Pharmacological Activities, Plant Metabolite, Therapeutic Uses

## 1. Introduction

Flora is currently the major source of both medicament and energy for humans. The primary features of plant metabolites are their high effectiveness and less adverse effects. Additionally, the biological systems of humans are negatively impacted by several synthetic substances. Natural sources include a variety of medicinal components, including terpenoids, flavonoids, glycosides, and alkaloids, that have the positive impact of preserving a healthy immune condition[1]. Natural sources include a variety of medicinal components, including terpenoids, flavonoids, glycosides and alkaloids, that have the positive impact of preserving a healthy immune condition[2]. Plants can produce a diversity of natural byproducts that are obligatory for modifying the behaviour of other living things. Currently, the most common issues impacting nature and our way of life are deforestation, UV radiation exposure, air pollution and water pollution, respectively[3]. Natural resources can help shield humans from these abiotic alterations. The main weapon in this

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condition's arsenal against many viruses, infections, bacteria and mutant strains is old folklore knowledge of plants and their metabolites[4]. Additionally, the rDNA method is being utilised to manufacture various secondary metabolites of complex architectures[5]. By definition, plants produce metabolites for specific functions like pollinator attraction or defence mechanisms, as well as essential functions like growth and development (primary metabolites)[6]. Furthermore, metabolites are organic compounds that come from an organism's chemical reactions that require enzymes for metabolism[7,8]. The main topic of this article is the pharmacological significance of some of the most important bioactive substances derived from plants.

All cells, including those of animals and plants, contain primary metabolites, which are essential to their development and growth[9,10]. Low molecular mass primary metabolites are crucial parts of agricultural plants for both farmers and consumers. A few of the most fundamental metabolites are amino acids, lactic acid and ethanol[11]. A basic metabolism characterised by balanced microbial growth is referred to as a "trophophase" which occurs when the medium has all the nutrients required by the organism[12]. Primary metabolism is necessary for both plant survival and cell division[13]. The cells contain the optimal amounts of all macromolecules, including proteins, Deoxyribonucleic Acid (DNA) and Ribonucleic Acid (RNA), during the trophophase[14]. The total metabolic waste products that all bacteria produce during the trophophase are known as primary metabolites[15]. Primary essential metabolites, such as vitamins, amino acids, and nucleosides, are those compounds produced in sufficient numbers to enable cellular growth. These two categories of primary metabolites are separated further. Since they were wasted, primary microorganisms often do not overproduce the necessary primary metabolites. When there is industrial overproduction, the regulatory mechanisms are activated[16,17] and the second is primary metabolic end products, which are the customary and typical byproducts of the fermentation process involved in primary metabolism. The end products have a large range of factory implementation, which includes acetone, lactic acid, as well as ethanol. To leaven bread during baking, Saccharomyces cerevisiae produces carbon dioxide as a metabolic byproduct[18].

Secondary metabolites can have flavours, colours and fragrances, but they typically combine with plant metabolites and organisms. Pollination can be assisted by a variety of creatures, including leaves, gastropods, caterpillars, fungi, bacteria, nematodes and viruses, in addition to animals like butterflies, bees, moths, and flies. When the bacteria's period of exponential growth ends, the idophase starts. The idiophase is defined by secondary metabolism[19]. Although the bacteria do not require secondary metabolites, they are very productive and have a variety of commercial uses, especially in the biotechnology sector where they are used to make plant hormones, steroids, antibiotics, alkaloids, glycosides, and poisons[20]. Particular microbes produce particular secondary metabolites. For an organism to develop and reproduce, secondary metabolites are not as important. The environment controls how they are produced. Certain microorganisms can produce many chemical molecules, rather than just one, that are secondary metabolites with similar structures. Streptomyces is one organism that manufactures anthracyclines as an example of this. Most secondary metabolites have poorly established pathways. The generation of these metabolites is regulated in greater detail than that of primary metabolites[21]. Two possible theories exist to explain the role of secondary metabolites. One holds that these molecules help cells survive, while the other holds that secondary metabolites are necessary for development. To control the overproduction of secondary metabolites and the metabolic regulation is difficult. Induction, catabolic regulation, phosphate control, bioconversions and self-regulation are a few examples of regulatory systems.

## 2. Pharmacological Activities of Plant-derived Alkaloids

Alkaloids are mostly found in flowering plants, and alkaloid plants with diverse chemical structures are extremely abundant. Alkaloids are made up of at least one nitrogen atom within an amine, indicating that they were created by replacing hydrogen atoms in ammonia to create hydrocarbons. Because it reacted with acids to generate salts, just like inorganic alkalis, the word "alkaloid" was derived from this property. Most alkaloids were composed of a cyclic

structure with several nitrogen atoms[22]. Alkaloids are colourless, crystalline, nonvolatile substances with a bitter taste; their names usually end in -ine. Alkaloids are classified (Table I) as having an indole ring system, and there are eight various types of alkaloids differentiated based on structure: pyrrolidine, pyrrolidine alkaloids, tropane alkaloids, pyrrolizidine alkaloids, isoquinoline alkaloid, an indole alkaloid, and quinoline alkaloid[23]. Based on various amino acids, such as tryptophan as well as phenylalanine, Hegnauer classified alkaloids into six further groups in 1963. Acridines, as well as amides, are the chemical-structural categories in which Price classified Rutaceae. The scientists' classification of family types served as the basis for this classification[24].

Three novel aporphine alkaloids, or xylopialoids, have been identified from the roots of *Xylopia vielana*, according to a more recent research contribution. With a 1.39Mm value of $IC_{50}$ versus MCF cell, the chemical 1-hydroxy aporphine derivative (1) shows potential inhibition against nitric oxide generation among these

**Table 1.** Various alkaloids, their resources and therapeutics use

| Alkaloid | Taxonomical name of plant (common name of plant) | Extract and part of the plant | Pharmaceutical Uses | Refe rences |
|---|---|---|---|---|
| References | *Papaver somniferum* (Opium poppy) | Methanolic Extract- Seed, Leaf | Narcotic pain reliever | 25 |
| Quinine | *Cinchona officinalis L.* (Jesuit's bark) | Methanolic Extract. - Bark | Antimalarial agent | 26 |
| Strychnine | *Strychnos nux-vomica* (Quaker button) | Methanolic Extract- Nut | Maintaining reflex action | 27 |
| Lobeline | *Lobelia inflata* (Indian tobacco) | Methanolic Extract- Leaves | Stimulation of the respiratory tract | 28 |
| Boldine | *Peumus boldus Molin* (Chilean boldo tree) | Methanolic Extract- Leaves | Stool softening | 29 |
| Aconitine | *Aconitum napellus* (Monkshood) | Methanolic Extract- Root | Neuron related pain | 30 |
| Ergometrine | *Fungus, Ergot (Claviceps purpurea)* (Ergonovine) | Methanolic Extract- Fungus | Facilitate childbirth | 31 |
| Ephedrine | *Ephedraceae Dumort* (Brigham tea) | Methanolic Extract- Dried Branches | Dilation of arteries in bronchospasm | 32 |
| Narceine | *Papaver somniferum* (Opium poppy) | Methanolic Extract- Seed, Leaf | Pain reliever | 33 |
| Atropine | *Atropa belladonna* (Deadly nightshade) | Methanolic Extract- Leaf | Anticholinergic drug | 34 |
| Caffeine | *Camellia sinensis* (Tea plant) | Methanolic Extract – Leaf | Affects the state of mind, mental awareness, and bodily and cognitive performance, as well as affects the heart, lungs, kidneys, and smooth muscles. | 35 |
| Pilocarpine | *Pilocarpus microphyllus* (*Jaborandi*) | Methanolic Extract- leaf | To treat glaucoma, excessive intraocular pressure, and dry mouth in addition to eye diseases | 36 |
| Solanidine | *Solanum americanum* (Green potatoes) | Methanolic Extract- Tuber | Acetylcholinesterase Inhibitors, Anti-HIV Activity, Anti-Cancer Activity | 37 |
| Hygrine | *Erythroxylon coca* (Coca leaves) | Methanolic Extract - Leaf | Gastrointestinal conditions such as irritable bowel syndrome, peptic ulcers, and spasms | 38 |
| Senecionine | *Jacobean vulgaris* (Ragwort) | Methanolic Extract- Flowers, Leafs | Treat dyspepsia, diabetes, and gout | 39 |

substances[40]. Additionally, *Clausena hainanensis* stems and leaves are used to extract five novel carbazole alkaloids known as clausehainanines. Compounds with a variety of isopentenyl derivatives substituting at the C-2 position (2) are among the unique carbazole alkaloids (Figure 1). Human adenocarcinoma of the colon (SW480), human carcinoma of the lung (A-549), individual hepatocarcinoma tumour line (SMMC-7721), human breast cell line (MCF-7), and Caucasian promyelocytic blood carcinoma (HL 60) are the five human tumour cell lines used to assess through in vitro antiproliferative activities of isolated compounds.

Most molecules showed promising effects on cell proliferation with a range from 0.120 to 15.560 μM of $IC_{50}$ value. These outcomes suggested the findings of alkaloids with carbazole nuclei showed cytolytic properties as new anticancer agents (Figure 1). This study shows that three known analogues and two recent epimeric tetrahydro-β-carboline alkaloids were isolated from the dry flower of *Carthamus tinctorius* Linn[41]. High-resolution electrospray ionization mass spectrometry and one/two-dimensional Nuclear Magnetic Resonance (NMR) spectroscopic data analyses are determined by the planar structure. Electronic Circular Dichroism (ECD) curves assess the absolute configurations of alkaloids. To measure the effect on melanogenesis, isolated alkaloids were tested against the tyrosinase enzyme. Tyrosinase was inhibited by the alkaloid 2-methylbut-2-en-1-ol (3), with a 0.170 μM $IC_{50}$ value, as opposed to 0.180 μM for arbutin[42].

Additionally, plants *Houttuynia cordata* Thunb provided the novel alkaloids houttuynamide B and C as well as houttuycorine. Using lipopolysaccharide activation and the murine macrophage cell line (RAW 264.7), all isolates were assessed for their ability to produce $NO_2$. With an $IC_{50}$ value of 8.70 μM, a molecule containing furfuryl alcohol side chain (4) had the strongest anti-inflammatory properties[43]. From Corydalis decumbens, novel alkaloids, 1R, 9S, 70S-O-methylegenine, 1S,9R,70S-O-methyl egenine, and 1S,9S,70S-O-methylegenine, were identified. Rat polymorphonuclear leukocytes released the enzyme β-glucuronidase at a concentration of 10 μM, exhibiting in vitro anti-inflammatory activity of 32.4–41.3%. Results indicated that one molecule, number five, had strong anti-inflammatory qualities and might successfully combat rheumatoid arthritis[44]. Another study reflects those two new alkaloids as (−) goniolanceolactam and 2-acetyl-3-amino-1,4-naphthoquinone along with two known naphthoquinone alkaloids 2-acetyl-3-amino-5-hydroxy-1,4-naphthoquinone and cleistopholine were separated from the root of *Goniothalamus lanceolatus* (*Annonaceae*) using its dichloromethane extract. Among them, one alkaloid (5, 6) showed cell-inhibiting activity on human colon and lung carcinoma activity with a 50% inhibitory concentration value from 5.320-9.910 μM.

The rare, glycosylated pyrrolidine moiety of nigellisoquinomine and nigellapyrrolidine, together with agrocybenine and 4,6,6-trimethyl-3,4-epoxypiperidin-2-one (7), were also isolated from *Nigella glandulifera*. One of the compounds, which has a unique pyrrolo-isoquinoline structure, had a strong 50% inhibitory effect on protein tyrosine phosphatase 1B at a dose of 3.65 μM[45,46]. The roots of *Stephania epigaea* were used to isolate a novel proaporphine alkaloid known as epiganine A and epiganine B, which together contain eight recognised alkaloids: pronuciferine, dehydrodicentrine etc. The ultimate arrangement was to be ascertained using electronic circular dichroism. Merely two substances connected to the isopropanenitrile group at the isoquinoline nitrogen exhibited potent inhibitory actions against acetylcholinesterase, with 50% inhibition concentration values of 4.36 and 2.98μM (8), in that order[47].

According to a different study, five novel amide alkaloids, together with one novel organic substance and four recognised alkaloid analogues, were extracted from the grain of *Clausena magnesium*. The structures of novel amide alkaloids were assessed using 1D NMR, 2D NMR, and HRESIMS. Compounds (9), on the other hand, demonstrated moderate nematicidal action with values of $IC_{50}$=0.12μM whereas compound (10,11) showed good nematicidal efficacy against *Panagrellus redivivus* with values of 2.75 and 3.93μM, respectively. While the control abamectin was observed with1.05 μM of $IC_{50}$ value. According to a recent study, the existence of the uracil guanidine groups, and the connected hydroxyl group demonstrates the mechanism of action of the endogenous alkaloids Cylindrospermopsin (CYN) to generate oxidative-related stress toxicity in eukaryotic cells. Three synthetic derivatives, including the tetracyclic analogue of CYN without a hydroxyl group at C-7, were created in this study employing uracil and guanidine as groups connected by a 4-6

carbon linkage each having a hydroxyl group. An *in vitro* model of human neutrophils taken from disease-free subjects was used to evaluate the toxicity of these compounds and was then compared with CYN and guanidinoacetate. The lowest activity was observed in the case of Reactive-Oxygen-Species (ROS) and lipid peroxidation as well and cell fatality was seen for acetic acid (glacial) and the tetracyclic analogue. The highest adverse effect was shown in the case of a 6-C chain length linker (12) (Figure 1) otherwise all three analogues and CYN were seen with rapid onset of redox imbalance[48].

Five novel gelsedine-type oxindole alkaloids, known as gelseleganins A to E, were identified from a 70% alcoholic extract of leaves and branches of Gelsemium elegans, according to phytochemical analysis. As characterisation tools for elucidating structures, 1H-1H-correlated Spectroscopy, Heteronuclear Multiple Bond Coherence NMR spectroscopy and Heteronuclear Multiple Quantum Coherence were

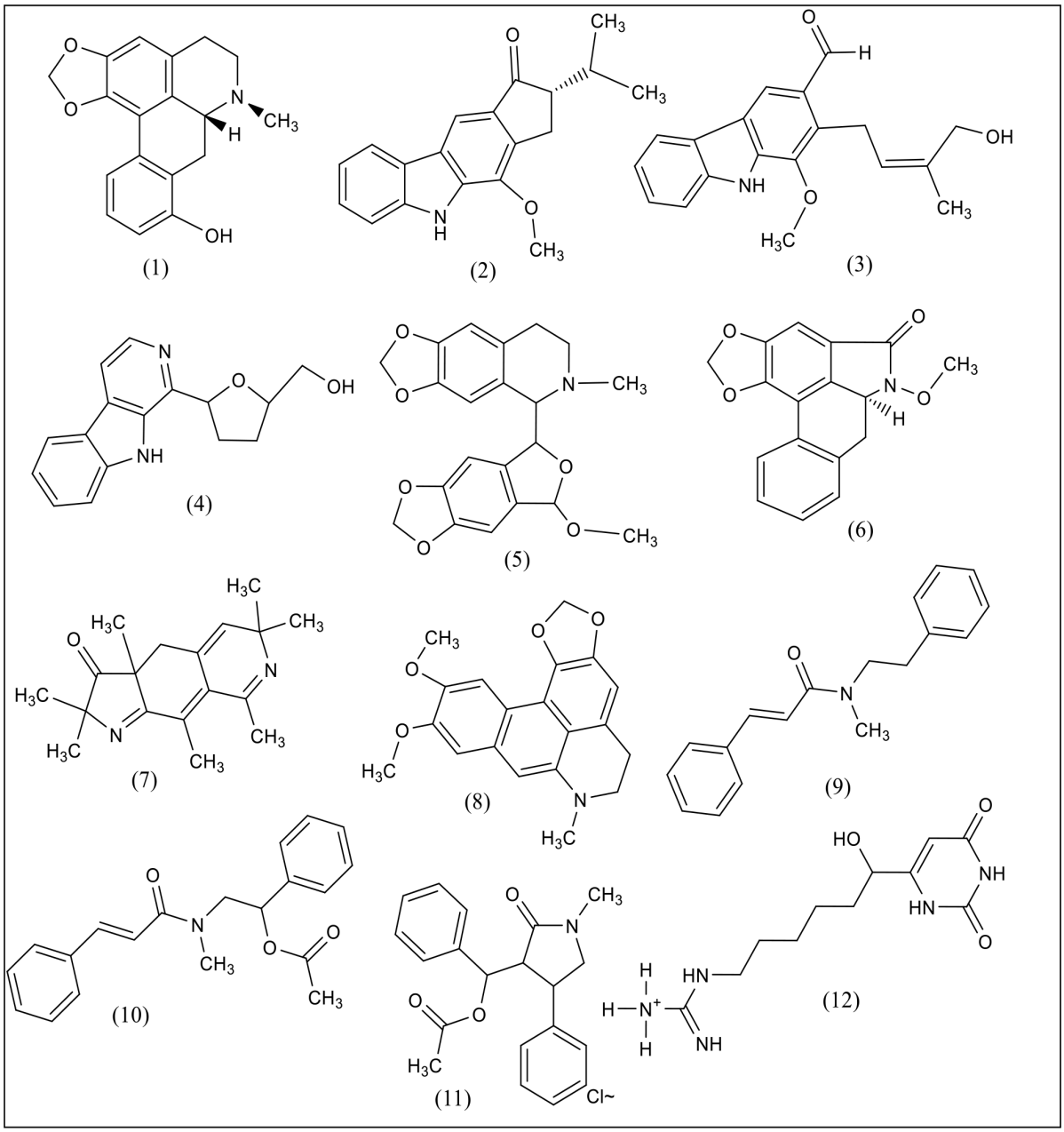



**Figure 1.** The chemical structure of some plant-based alkaloids (part A).

employed. The cytotoxic effect of the material was judged in vitro on seven tumour cell lines. Results showed that one alkaloid (13) (Figure 2), with $IC_{50}$ value less than 10μM. demonstrated good cell toxicity properties against the tumour cell line[49]. A recent study found that an 80% ethanolic extract of the leaf and other parts of *Kopsia hainanensis* yielded five new aspidofractinine-type alkaloids, named kopsiahainins A–E. Structural elucidation was achieved through one-dimensional and two-dimensional NMR, Infrared (IR), UV and High-Resolution Electrospray Ionisation Mass Spectrometry (HR-ESIMS). Among these, two alkaloids (14,15) demonstrated cytotoxicity against various human tumour cell lines, including hepatic (HepG2), breast (MCF-7), gastric (SGC-7901), melanoma (SK-MEL-2) and ovarian (SK-OV-3) with $IC_{50}$ values ranging from 7.3 to 10.6 μM. Molecular interactions of *Peganum harmala* alkaloids with the myeloperoxidase enzyme were studied using the GlideXP docking protocol, and the redox potential was measured using an epsilon potentiostat. HPLC was employed to evaluate the amount of harmala alkaloids. The study revealed β-carboline alkaloids such as harmaline, harmane, harmol, harmalol (16) and harmine (17) as potent myeloperoxidase inhibitors with $IC_{50}$ values of 0.26, 0.08 and 0.72 μM respectively.

Another investigation evaluated the antimicrobial and free radical scavenging properties of *Hammada scoparia* extracts and their essential alkaloids using the following methods: 2,2-diphenyl-1-picrylhydrazyl (DPPH), β-carotene–linoleic acid system, and decreasing activity. The aqueous ethanolic extract exhibited the highest scavenging activity ($EC_{50}$=24 μg/mL) and strong β-carotene–linoleate inhibition. All

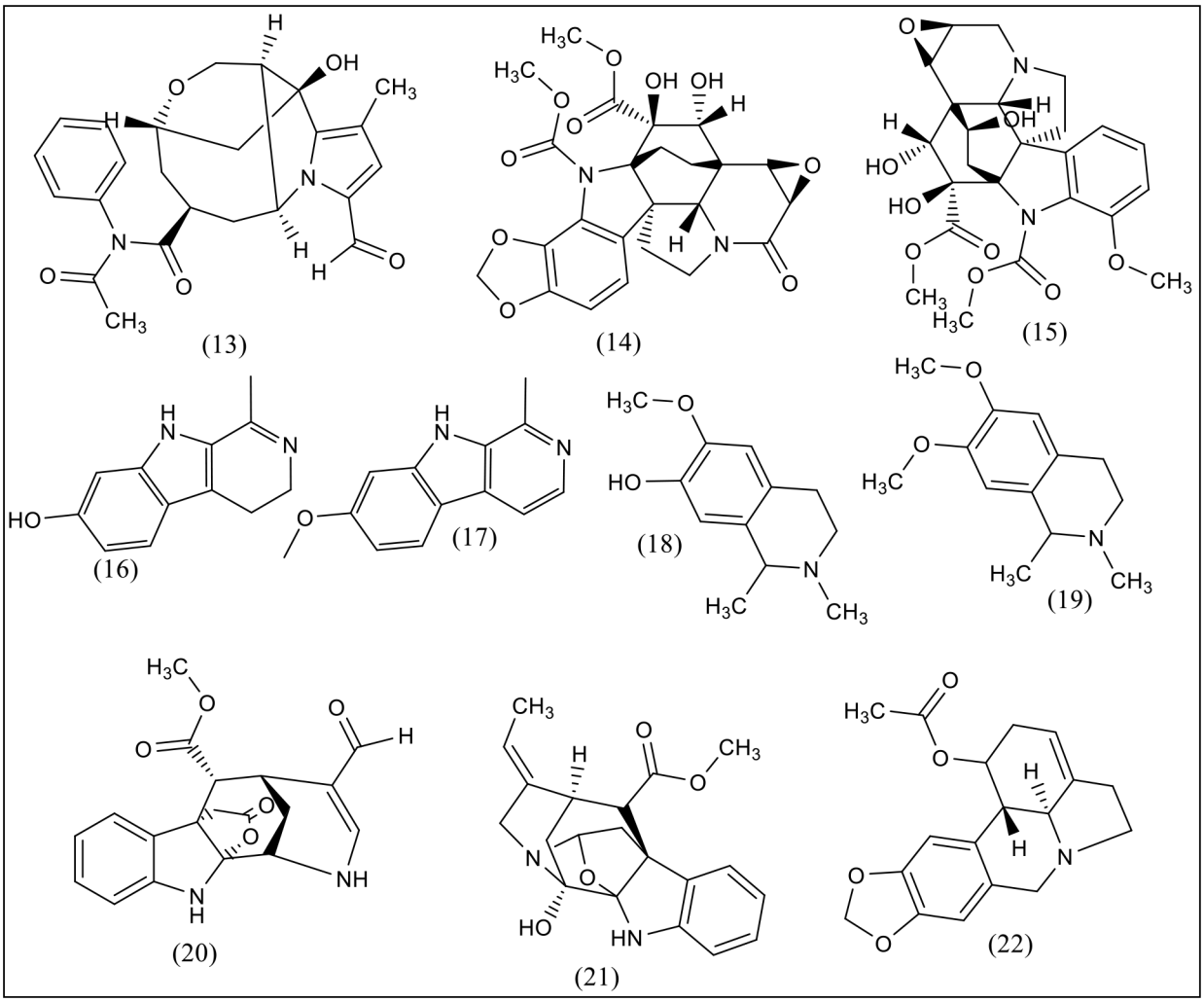



**Figure 2.** The chemical structure of some plant-based alkaloids (part B).

extracts, except those derived from hexane, showed significant microbial inhibition against both gram-positive and gram-negative microorganisms, with inhibition zones ranging from 8 to 30mm. The main compounds, carnegine (18) and N-methylisosalsoline (19) demonstrated the most potent bactericidal and antioxidant properties. Additionally, a study on the fruit of *Alstonia scholaris* isolated a new nor-monoterpenoid indole alkaloid for its cytotoxic effects on human glioma stem cells. *A. scholaris* showed a high content of monoterpenoid indole alkaloids effective against glioma stem cells, characterised by phenotype screening and MTS assays. The structures were determined using UV, IR, NMR and mass spectroscopic spectra. The findings indicated selective antitumor activity against glioma stem cells, with compounds 3.0, 12 and 18 showing $IC_{50}$ values of 15-25μM (20, 21), by inducing programmed cell death and enhancing the expression of tumour necrosis factor-alpha and caspase-3 enzyme cleavage. Moreover, bioassay-guided fractionation of *Amaryllis belladonna* bulbs led to the separation of a novel crinane alkaloid, 1,4-dihydroxy-3-methoxy powellan, together with three already discovered crinane alkaloids (22) lycorane alkaloids. The structures were characterised using HR-ESIMS, Circular Dichroism (CD) and 2D-NMR spectroscopic data. Among these, acetylcaranine, one lycorine-type alkaloid, exhibited strong antiplasmodialactivity[50-53].

## 3. Pharmacological Activities of Plant-derived Glycosides

Glycosides are produced with one or more sugar moieties and the aglycone part is made up of either terpene, flavonoid, coumarin, or some other kind of natural substance. D-glucose is the most prevalent sugar component in natural glycosides, followed by L-rhamnose and L-fructose, which is also rather common. L-arabinose is the more prevalent pentose sugar than D-xylose[54]. This categorisation of glycosides is based on the glycosidic linkage. Chemically, glycosides are typically mixed acetals with a nucleophilic atom-containing moiety in place of the hydroxyl group on the anomeric carbon. According to Nahrstedt *et al.*, the glycone portion of a glycoside is connected to the aglycone portion via the atoms of oxygen, carbon, nitrogen and sulphur (referred to as O-glycosides, C-glycosides etc) (Table 2). Cyanogenic glycosides,

**Table 2.** Various glycosides, their resources and therapeutics uses

| Glycoside Type | Name of Glycoside | Source Taxonomical Name (Source Common Name) | Extract and Part of Plant | Therapeutic Use | References |
|---|---|---|---|---|---|
| **Cyanogenic** | Amagdalin | ***Prunus Amygdalus*** (Almonds) | Hydroalcoholic-seed | Cancer | 55 |
| | Linamarin | ***Linum usitatissimum*** (linseed) | Hydroalcoholic-seed | Anti-cancer drug | 56 |
| **Anthraquinone** | Frangulin A | ***Rhamnus frangula*** - | Hydroalcoholic-bark | Anti-inflammatory | 57 |
| | Sinnoside A and B | ***Senna alexandrina*** (Candle Bush) | Hydroalcholic-leaves | Laxative | 58 |
| | aloin A and aloin b, aloe | ***Aloe barbadensis*** (Aloe vera) | Hydroalcoholic-leaves | mild burns | 59 |
| **Cardiac** | Digitoxin | ***Digitalis purpurea*** (Foxglove) | Hydroalcoholic-flowers | It has a beneficial inotropic impact on failing heart and is useful in atrial fibrillation treatment. | 60 |
| | lanatoside C and diacetyl-lanatoside C. | ***Digitalis lanata*** (Grecian foxglove) | Hydroalcoholic-leaves | Antiarrhythmic agent | 61 |
| **Alcohol** | salicin | ***Salix fragilis*** - Crack willow | Hydroalcoholic-bark | Anti-inflammatory, antioxidant, anticancer | 62 |
| **Isoprenoids** | diosgenin and hecogenin | *Trigonella foenum-graecum* (fenugreek) | Hydroalcoholic -leaves and stem | Cancer, diabetes, arthritis | 63 |

Anthraquinone glycosides, Cardiac glycosides, Alcohol glycosides, Isoprenoid glycosides and Isothiocyanate glycosides are some of the numerous forms of glycosides.

According to a different study, *Leonurus japonicus* (*Lamiaceae*) contains a significant number of phenolic glycosides such as lihroside, leonurusoside C, 2000-syringoylrutin, rutin and lavanduliofolioside which are utilised as potent anti-Alzheimer's medications because they have anti-acetylcholinesterase (anti-AChE) activity. These five glycosides are hydrolysed to produce hydroxytyrosol, p-coumaric, caffeic, quercetin and syringic acid. $IC_{50}$ values demonstrated by Caffeic acid (23) and quercetin were 1.05µM and 3.58µM, respectively. With 9.18 mg/g as determined by HPLC, rutin emerged as the predominant flavonoid present within the extract[64]. The A549 cell line, originating from lung cancer, was utilised for determining pathways involving antiapoptotic properties by cardenolide glycosides. This characteristic was evaluated using the annexin V-Fluorescein Isothiocyanate (FITC) method with PI staining. The mitochondrial membrane depolarisation was analysed through JC-1 labelling. Absolute regioselectivity for the 19-position of andrographolide was shown by α-galactosidase. With a minimal inhibitory concentration of 8 g/ml, the glycosylated andrographolide (24) demonstrated antimicrobial activity against typical species of food/water-borne bacteria[65]. The rhizome of *Curculigo orchioides* yielded orcinosides I through J, as well as seven novel phenolic glycosides, five chlorophenolic glycosides, curculigines J through N and nineteen other recognised chemicals[66]. The structures were characterised using 1D and 2D NMR, HRESIMS, UV, IR, and HRESIMS. In a study by Chen *et al*., orcinoside I (25) and orcinoside J demonstrated inhibition of xanthine oxidase, with values recorded at 0.25µM and 0.62µM,( $IC_{50}$) respectively. Scugalerosides A and B as new flavanone glycosides were obtained from *S. galericulata*[67]. *In vitro,* anti-swelling activities of the glycosides (26, 27) were observed with proper inhibition of β-glucuronidase enzyme release from leukocytes of rats at concentrations of 10µM. Clausenaglycosides A–D as new phenylpropanoid glycosides amalgamated with known compounds and obtained from *Clausena dunniana* var. *robusta*[68]. 1-D and 2-D NMR, mass spectroscopy, along with circular dichroism data were used to characterise the isolated compounds (28, 29). The NF-κB inhibitory activity was determined in HeLa cells. Among them, one compound was observed with a mild blockage for NF-κB activation. Different types and parts of chestnut (Japanese horse) were used as a source of antioxidants. As per the presence of proanthocyanidins, seed shells were observed with a huge concentration of antioxidative components. Also, peeled seeds were primarily contained with flavonols (quercetin, kaempferol) at 66.7% concentration and then participated in antioxidative behaviour. The extract of whole seeds was observed with the identification of kaempferol, quercetin, and flavonol O-glycosides (eight) as the aglycone part. The outcomes indicated that seeds (peeled) were used as suppliers of flavonol O-glycosides (30) for additives and dietary supplements[69]. According to this work, a new class of anticancer compounds called berbamine glycosides was created using the glycosyl production method. For testing the *in vitro* cytotoxic activity of the glycosides, the human leukaemia (K562) cell line, human lung adenocancer (A549) cell, and mouse lymphocytic leukaemia (L1210) cells were utilised. Based on the findings, berbamine and its glycosides (31) (Figure 3) were shown to be cytotoxic, and their derivative (acetyl glycosyl berbamine) had strong action[70]. *Asclepias subulata*, contains several cardenolide glycosides including desglucouzarin, corotoxigenin 3-O-glucopyranoside, calotropin and 12, 16-dihydroxycalotropin. All these substances show significant antiproliferative action against the A549 malignant cell cultures, LS180 and PC-3 in the MTT experiment. Calotropin is the most active of them, with values of 0.00130, 0.060 and 0.410 µM ($IC_{50}$) respectively[71]. Corotoxigenin-3-O-glucopyranoside and esglucouzarin show $IC_{50}$ values within the scope of 2.3-6.1 µM against the same cell lines. According to these findings, human malignant cells, normal cells and murine malignant cells were more sensitive to calotropin (32)[72]. In 2013, Dr. Li isolated denneanosides A–E as five new phenanthrene glycosides and a novel 9,10-dihydrophenanthrene glycoside known as denneanoside F (33) isolated from the stem of *Dendrobium denneanum. Ex vivo* evaluation was conducted to assess cytotoxic activity against the SNU387 hepatocellular carcinoma cell line was evaluated and among them, three compounds exhibited moderate cytotoxic activities and the rest showed weak activities[73]. *P. marsupium* and *U. wallichiana* were used to isolate various phenolic C-glycosides and some were obtained from sugar and phloroacetophenone using scandium (III) triflate in

ethanol, water mixture and evaluated their anti-hyperglycemic activity by *in vitro*, *in vivo* process related to uptake of glucose by rodent (rat) muscle cell cultures and streptozotocin-induced (small dosage) diabetic rodent (rat) sequentially. Among them, eight compounds demonstrated a notable reduction in blood sugar levels in low-dosed-streptozotocin-induced diabetic rodents (mice). At a dose of 25 mg/kg body weight, one molecule (34) showed efficiency in lowering blood glucose levels (34.9%, 33.6%) during periods of (0–5) h and (0–24) h, respectively as compared to standard molecule metformin[74]. Yokosuka *et al.* used the underground portion of *Y. glauca* (*Agavaceae*) to isolate six steroidal glycosides and 14 known compounds. 2D nuclear magnetic resonance data was employed to define the structures and evaluated against human carcinomas (HL 60) cell lines and human lung adenocarcinoma cells (A549). Among them, (four) spirostanol and (three) furostanol glycosides were observed with cell toxic properties and showed apoptotic behaviour against human leukaemia cell lines[75]. Nguyen and his co-workers procured eleven flavonoid glycosides (cleome sides C-M) together with known compounds and their ester derivatives of quercetin or kaempferol from the aerial part of *C. chelidonii*. Spectroscopic data was used to characterise all structures. Antioxidative behaviour was confirmed by

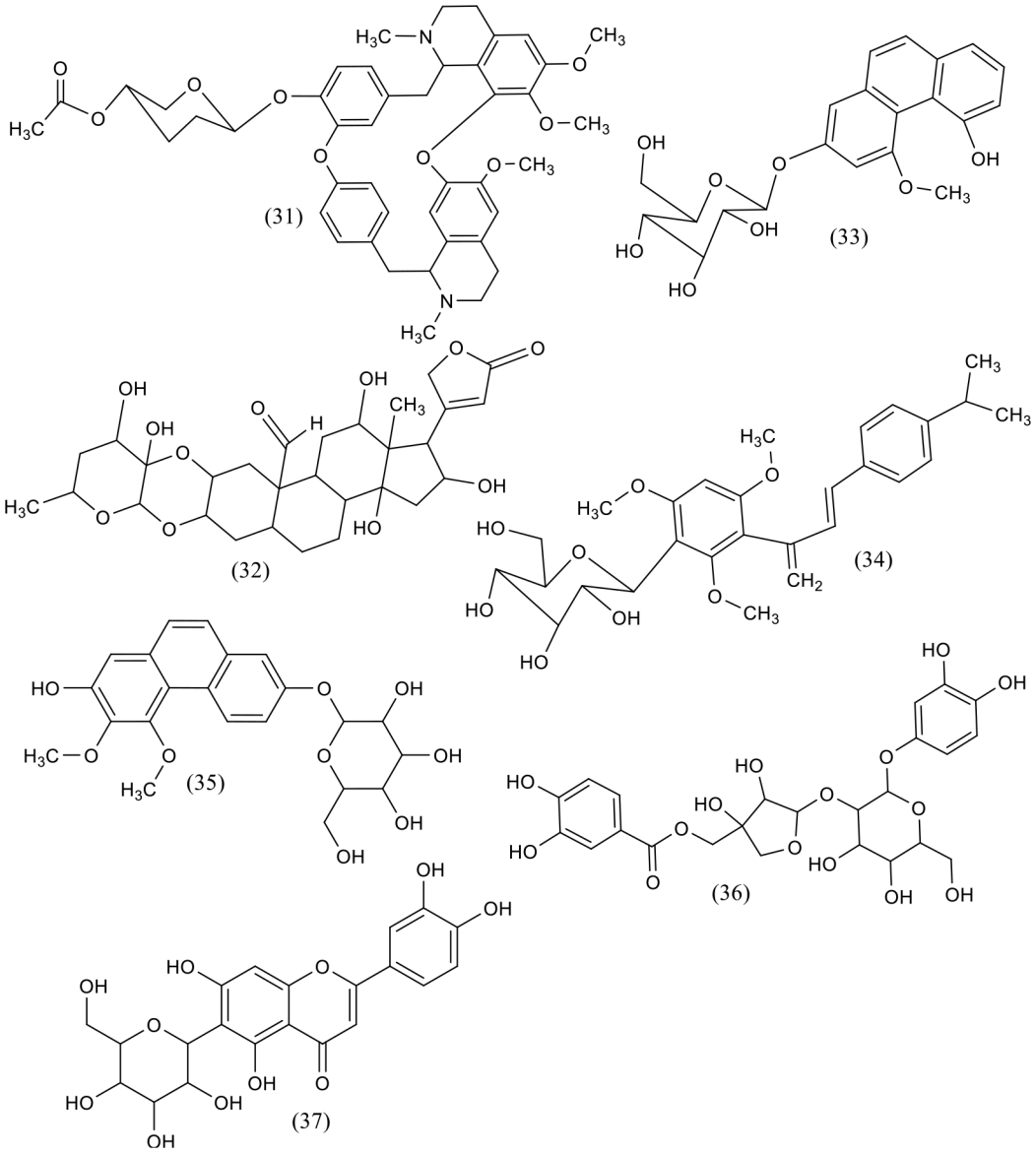



**Figure 3.** The chemical structure of some plant-based glycosides.

DPPH radical scavenging methods by considering quercetin and kaempferol aglycones. The presence of rhamnose (acetate derivative) produced the strongest antiradical activity[76]. New generation (spiroorthoester) pregnane glycosides as 3-O-formyl-periploside F and periplosides (W-Y) isolated from *Periploca chrysantha* and all of the four new pregnane glycosides showed significant inhibition against B and T lymphocytes and B lymphocyte proliferation as compared to cyclosporin A[77]. Nudolglycosides (A and B) and a series of known molecules as phenanthrene glycosides were isolated from *Liparis regnieri* Finet and MS, NMR spectroscopic data were used to characterise their structures; extracts showed bacterial growth inhibition against *E. faecalis*, *B. subtilis, R. anatipestifer*, *S. gallinarum*, *S. agalactiae, S. aureus* and *V. parahemolyticus*. Among them, some phenanthrene derivatives (35) showed significant microbial inhibition against *S. agalactiae* and *B. subtilis* accompanied by $IC_{50}$ values in the range of 48.0-54.4 μM[78]. Radicles of *Tecoma mollis* yielded three novel phenolic glycosides and 9 known glycosides, which were assessed for their DPPH radical scavenging activity through detailed spectroscopic analysis to determine their structures. The isolated compounds underwent evaluation for their antioxidant properties, inhibition of the cyclooxygenase-2 enzyme, and cell toxicity activities. Among these compounds, one (36) demonstrated significant antioxidant effects holding a value of 8.7μM ($IC_{50}$), comparable to ascorbic acid. Additionally, three compounds showed notable cyclooxygenase-2 inhibition with $IC_{50}$ values of 11.30μM, 9.400μM, and 13.40μM, respectively[79]. In another study, Jin isolated three new pregnane glycosides and four known compounds from the methanolic extract of *Cynanchum atratum*. These components were identified using extensive 2D NMR and were evaluated for their potential to inhibit B16 melanoma cells' melanogenesis activated by stimulating hormone α-melanocyte. One compound (37) exhibited a dose-dependent inhibition of melanin production and $IC_{50}$ values ranging from 4 to 33 μM[80-82].

## 4. Conclusion

From the ancient knowledge of plants, plant materials have been used to conquer disease. Initially, the whole plant was used but scientific knowledge is now used to isolate the principal constituent(s) as alkaloids and glycosides. The structure elucidation of these secondary metabolites helps to identify the exact structure of the metabolite, responsible for their activities which range from antioxidant and antimicrobial to anticancer. The main advantages of these plant metabolites are specific activity along with fewer side effects. However, the main limitation of these metabolites is that they are not cost-effective due to their isolation process. So, in the present scenario, scientists are focusing on the semi-synthetic way to synthesise the exact chemical entity. If we focus our resources and scientific minds on plant metabolites, they can be used as a principal source of medicines for various disease treatments.

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## 6. Author Contribution

Supriyo Saha, Sonali Patil-Shinde: conceptualization, design, and literature search; Prinsa, Chinmay Mali: Writing, editing, literature search; Saloni Srivastava: editing, drafting review; Sohan Chitlange: review and verification. All authors have read and agreed to the published version of the manuscript.

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