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Solanum alkaloids and their pharmaceutical roles: a review

Abstract

The genus *Solanum* is treated to be one of the hypergenus among the flowering families and is comprised of about 1500 species with at least 5000 published epithets. The genus is well represented in the tropical and warmer temperate regions. About 20 of these *Solanum* species are endemic to the northeastern region. Many *Solanum* species are widely used in popular medicine or as vegetables. The presence of the steroidal alkaloid solasodine, which is potentially an important starting material for the synthesis of steroid hormones, is characteristic of the genus *Solanum*. Soladodine, and its glocosylated forms like solamargine, solosonine and other compounds of potential therapeutic values.

Keywords: *solanum*,steroidal alkaloid, solasodine, hypergenus, glocosylated, injuries, infections

Volume 3 Issue 6 - 2016

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Received: October 21, 2016 | **Published:** December 15, 2016

Abbreviations: TGA, total glycoalkaloid; SGA, steroidal glycoalkaloid; SGT, sergeant; HMG, hydroxy methylglutaryl; LDL, low density lipoprotein; ACAT, assistive context aware toolkit; HMDM, human monocyte derived macrophage; CE, cholesterol ester; CCl_4, carbon tetrachloride; 6-OHDA, 6-hydroxydopamine; IL, interleukin; TNF, tumor necrosis factor; DPPH, diphenyl-2-picryl hydrazyl; FRAP, fluorescence recovery after photobleaching; O_2, oxygen, H_2O_2, hydrogen peroxide; SCVs, small colony variants; PC, prostate cancer; TNFR, tumor necrosis factor receptor; TIMP, tissue inhibitor of metalloproteinase; EMMPRIN, matrix metalloproteinase; BAECs, bovine aortic Endothelial Cells; HPTLC, high performance thin layer chromatography; HPLC, high performance liquid chromatography; DNP, dictionary of natural products; CNS, central nervous system

Introduction

Medicinal plants usage for the treatment of diseases, injuries, infections, health benefits and disease management is age old as mankind. Ethnic medicine is the sum total of knowledge and practical application, whether explicable or not, used in diagnosis, prevention and elimination of disorders which is handed over from generation to generation orally or in scripts. Recently, World Health Organization imitated programmes to promote and develop this indigenous medicine in health care systems and also to integrate this ethnic herbal medicine with modern to revitalize and strengthen the manpower.[1] The medicinal properties of herbals are attributed by their rich pool of diverse phytochemicals distributed within them. The major class of phytochemicals identified in plants with remarkable therapeutic properties includes the categories such as alkaloids and polyphenols.

Species of *Solanum* are widely used in health care systems and represents a source for diverse phytochemicals including alkaloids. Since decades, *Solanum* alkaloids have been a topic of interest in pharmacological and therapeutical studies because of the wide range of biological activities such as antimicrobial, antirheumatics, anticonvulsants, anti-inflammatory, antioxidant and anticancer. Further, these alkaloids are of paramount importance in drug industries as they serve as precursors or lead molecules for the synthesis of many of the steroidal drugs which have been used for regulating inflammation, menopause and in cardiovascular treatments. This review aims to encompass various strategies employed for the isolation, purification, characterization and medicinal values of *Solanum* alkaloids. In addition, the information related with medicinal relevance of these molecules leads future scientific exploration for the development of new and effective therapeutic drugs are also discussed.

Origin of the word alkaloid

The word alkaloid was framed by Meisner et al.,[2] in 1819 from alkaline refers 'alkali-like'. Alkaloids are cyclic compounds of biological origin with nitrogen atom attached to at least two carbon atoms. The nitrogen may exist as primary, secondary, tertiary or quaternary amine form. Mostly, the alkaloids are crystalline and colourless with exceptions like coniine, pilocarpine and nicotine (liquid) and berberine, colchicines (yellow) and canadine (orange). These natural organic molecules provide positive response with specific reagents in qualitative analysis as shown in Table 1.[3]

Narcotine is believed to be the first alkaloid isolated in 1803,[4] followed by morphine in 1806.[5] Dictionary of Natural Products documented a pool of alkaloids comprising approximately 27,683 types.[6] Generally, in plants alkaloids provide defense against pest, pathogen and herbivory. Majority of the alkaloids are weak bases, but some like theobromine and theophylline are amphoteric. Solubility of alkaloids in water is poor but dissolves in organic solvents like diethyl ether, chloroform or petroleum ether. Examples of water soluble alkaloids are caffeine, cocaine, codeine and nicotine (with a solubility of ≥1g/L), while others like morphine and yohimbine are less water soluble (0.1–1g/L). Alkaloids and acids form salts of different strengths and these derived products are usually soluble in water and alcohol and less soluble in organic solvents except scopolamine hydrobromide and the water-soluble quinine sulphate. Majority of alkaloids have a bitter taste and are poisonous.

Distribution of alkaloids

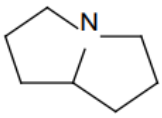
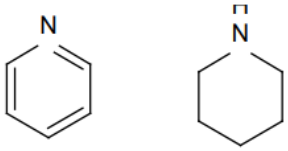
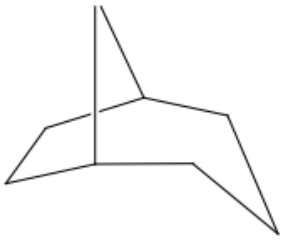
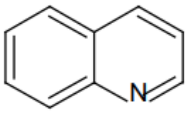
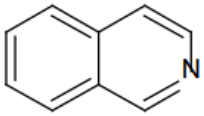
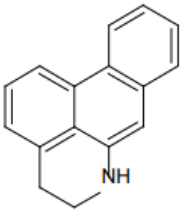
Alkaloids are reported mostly from angiosperms (10 to 20% and more among dicots than monocots) followed by gymnosperms, pteridophytes and fungi. Interestingly animals and microbes are also known to produce alkaloids. The common alkaloid bearing families were *Chenopodiaceae, Lauraceae, Magnoliaceae, Berberidaceae, Menispermaceae, Ranunculaceae, Papaveraceae, Fumariaceae, Papilionaceae, Rutaceae, Apocynaceae, Loganiaceae, Rubiaceae, Boraginaceae, Convolvulaceae, Solanaceae* and *Campanulaceae*.

Based on the plant species, the highest concentration is noticed in the leaves (black henbane), fruits or seeds (Strychnine tree), root (*Rauwolfia serpentina*) or bark (cinchona). However, different cells of the same taxa may possess diverse alkaloids.

Table 1 Qualitative identification of alkaloids

Test	Reagent Composition	Positive Colour Change
Dragendorffs Reagent	Potassium bismuth iodide	Reddish-brown
Mayer's Reagent	Potassio mercuric iodide	White or pale yellow ppt
Hager's Reagent	Picric acid	Yellow
Wagner's Reagent	Solution of iodine in potassium iodide	Yellow or brown ppt.
Murexide Test (for Caffeine and Other Purine Derived Alkaloids)	Potassium chlorate + drops of HCl. Expose the resultant to NH3	Purple colouration

Table 2 Types of heterocyclic alkaloids with examples

Sl No:	Name	Structure	Examples
1	Pyrrole and Pyrrolidine	 Pyrrole Pyrrolidine	Hygrine; Stachydrine
2	Pyrrolizidine		Senecionine; Echimidine; Symphitine; Seneciphylline
3	Pyridine and Piperidine	 Pyridine Piperidine	Arecoline; Ricinine; Trigonelline; Anabasine; Pelletierine; Lobeline; Nicotine; Piperine; Coniine
4	Tropane (piperidine/N-methyl-pyrrolidine)		Cocaine; Atropine; Hyoscyamine; Hyoscine; Meteloidine
5	Quinoline		Quinine; Quinidine; Cinchonine; Cinchonidine; Cuspareine
6	Isoquinoline		Morphine; Emetine; Papaverine; Narceine; Narcotine; Tubocurarine; Codeine; Berberine; Galanthamine; Corydaline; Hydrastine; Cephaeline; Erythraline
7	Aporphine (reduced isoquinoline/ naphthalene)		Boldine

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DOI: 10.15406/japlr.2016.03.00075

Table Continued...

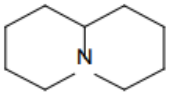
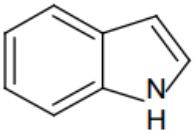
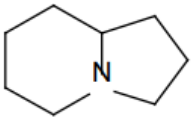
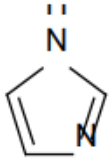
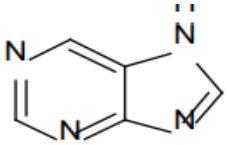
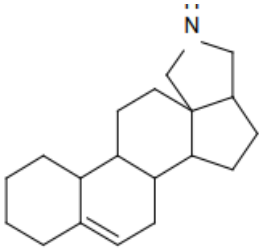
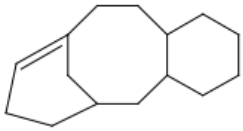
Sl No:	Name	Structure	Examples
8	Quinolizidine		Lupanine; Cytisine; Laburnine; Sparteine
9	Indole or Benzopyrole		Ergometrine; Ajmaline; Calabash; Vinblastine; Vincristine; Strychnine; Brucine; Ergotamine; Serpentine; Yohimbine; Physostigmine; Reserpine
10	Indolizidine		Castanospermine; Swainsonine
11	Imidazole or glyoxaline		Pilosine; Pilocarpine
12	Purine (pyrimidine/imidazole)		Theobromine; Caffeine
13	Steroidal (some combined as glycosides)		Conessine; Solanidine; Funtumine; Veratramine
14	Terpenoid		Aconitine; Atisine; Lycaconitine; Aconine

Table 3 Plant alkaloids and their biological activities

Sl.No	Biological Activities	Alkaloids	Sources
1	Hallucinogen	Bufotenine Muscarine	*Amanita* (Agaricaceae)
2	Alzheimer disease	Galanthamine	*Galanthus* (Amaryllidaceae)
3	Antimalarial	Alstonine Akuammigine Berberine	*Alstonia* (Apocynaceae)*Picralima* (Apocynaceae) *Berberis* (Berberidaceae)
4	Tranquillizer	Reserpine	*Rauwolfia* (Apocynaceae)
5	Anticancer	EllipticineVinblastine Vincristine Vindesine Pacletaxel	*Ochrosia* (Apocynaceae) *Catharanthus* (Apocynaceae)*Taxus* (Taxaceae)
6	Aphrodisiac	Yohimbine	*Yohimbe* (Apocynaceae)
7	CNS stimulant	Cathine	*Catha* (Campanulaceae)
8	Insecticidal	Anabasine Cevadine	*Anabasis* (Chenopodiaceae) *Schoenocaulon* (Liliaceae)
9	Antiviral	Calystegines	*Calystegia* (Convolvulaceae)
10	Local anaesthetic	Cocaine Loliine	*Coca* (Erythroxylaceae) *Lolium* (Graminae)
11	Induces polyploidy	Colchicine	*Colchicum* (Liliaceae)
12	Antihypertension	Rubijervine	*Veratrum* (Liliaceae)
13	Anthelmintic	Arecoline	*Areca* (Palmae)
14	Diuretic	Chelerythrine	*Dicentra* (Papaveraceae)
15	Analgesic Narcotic	Codeine Morphine	*Papaver* (Papaveraceae)
16	Parkinson disease	Tigloidine	*Duboisia* (Solanaceae)
17	Preoperativetreatment	Hyoscyamine	*Duboisia* (Solanaceae)
18	Antiarrhythmia	Quinidine	*Cinchona* (Rubiaceae)
19	Amoebic dysentery	Emetine	*Cephaelis* (Rubiaceae)
20	Cough suppressant	Narcotine	*Papaver* (Papaveraceae)

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Classification

Alkaloids are large class of nitrogen containing compounds differ in terms of structure, synthesis and biological activity. Therefore different classifications are available in alkaloids based on some criteria. Generally, alkaloids are classified based on:

a. Biosynthetic pathway based on the precursor used for synthesis,

b. Chemical classification-based on chemical entity,

c. Pharmacological classification-based on specific pharmacological properties and

d. Taxonomic classification-based on distribution of alkaloids in different plant groups.

Alkaloids are grouped into six based on the nature of amino acid from which it initiates its biosynthesis (namely anthranilic acid, ornithine, lysine, histidine, phenylalanine and tryptophan). Another system of classification includes nine categories based on chemical structure: acridines, amides, amines, benzylisoquinolines, canthinones, imidazoles, indolquinazolines, furoquinolines and quinazolines.[7] Further, a chemotaxonomic approach in alkaloid classification was also available.[8] Another classification of alkaloids was true, pseudo and proto alkaloids characterized with heterocyclic nitrogenic bases derived from amino acids or heterocyclic nitrogen base is not derived from amino acids or they are basic amines derived from amino acids, but nitrogen is not part of aromatic system (e.g. vanillylamid). A more practical system of classification includes a heterocyclic and non-heterocyclic group corresponding to whether or not nitrogen is a part of cyclic ring system.[9]

Heterocyclic alkaloids or typical alkaloids

This represents the largest group in which the nitrogen becomes a part of the cyclic ring system. It is further subdivided into 14 groups (Table 2).

Non-heterocyclic alkaloids or a typical alkaloids

In the case of non-heterocyclic alkaloid division nitrogen is not a part of the ring system and is relatively less common. Alkaloid of this category includes hordenine, erythromycin, ephedrine, colchicine, jurubin, pachysandrine-A, mescaline, taxol and a few others.

Biological potentials of alkaloids

Alkaloids can be considered as one of the best studied class of phytochemicals especially in taxonomic and pharmacological fields. Chemotaxonomists apply this in resolving taxonomic confusion among and within the taxa. Meanwhile, pharmacologists use the bioactive principles in ameliorating simple to complex multifaceted diseases. Many of the known alkaloids are noxious, some are addictive (morphine, cocaine) while, a few have clinical applications.[6,10] Table 3 narrates the bioactive alkaloids and their source from which they were isolated.

The nitrogen containing molecules of plant origin have served as scaffold in designing of cough suppressant drugs or drugs used for more chronic disorders such as Parkinson's and cancer (Table 4). Unfortunately, the total number of alkaloids that were marketed as prescribed drugs accounts to less than 0.002% of the total alkaloids in the Dictionary of Natural Products (DNP) list. In the last 20-25years, galanthamine and taxol were the newly introduced drugs in the global pharmaceutical armamentarium.[6]

Solanum as source of alkaloids

Many studieshave shown *Solanum* species as a rich store of diverse alkaloids.[11] In pharmacological studies, these compounds have exhibited promising biological activities both *in vitro* and *in vivo*. Further, drug manufacturers have made use of these alkaloids as lead molecules in the synthesis of novel steroidal drugs for various treatments (Table 5).

Steroidal glycoalkaloids are a class of glycosidic compounds derived from nitrogen-containing steroids. Structurally it consists of C27 cholestane skeleton to which 1 to 5 sugar moiety is attached at the 3-OH region of the aglycone. The monosaccharides comprise D-glucose, D-galactose, D-xylose and L-rhamnose and many others. Since, nitrogen is inserted into a non–amino acid; these molecules belong to a subclass of pseudo-alkaloids-isoprenoid alkaloids. The structural diversity of glycoalkaloids is confined to two major groups that are based on their aglycone skeleton. The spirosolan category is made up of tetrahydrofuran and piperidine spiro-linked bicyclic system with an oxa-azaspirodecane structure (as in solasodine) and the solanidane type is derived by an indolizidine ring where tertiary nitrogen connects the 2 rings (as in solanidine). In these molecules, nitrogen can be bonded as a primary amino group (free or methylated), which forms simple steroidal bases, ring-closed to skeletal as secondary NH or in two rings as a tertiary *N*, which often regulates the chemical character of the molecule. Glycoalkaloids always contain double bonds and OH groups in various positions. Nearly 90 structurally unique steroidal alkaloids were reported from 350 *Solanum* species.[11]

The major molecules of glycoalkaloid are α-solanine and α-chaconine in *S. tuberosum* and solasonine and solamargine in *S. melongena*, whereas α-tomatine and dehydrotomatine are spirosolane-type glycoalkaloids that occur in *Lycopersicon esculentum*. *S. tuberosum* produces α-chaconine and α-solanine, which share a common aglycone, solanidine, to which a trisaccharide moiety, either chacotriose (α-chaconine) or solatriose (α-solanine), is connected. Similar molecules are attached to the aglycone, like solasodine in the egg plant, thereby producing the glycoalkaloids solamargine and solasonine. Tomato species produces α-tomatine and dehydrotomatine, which differ only in terms of presence or absence of a double bond in the ring structure. Cultivar potato contains α-solanine and α-chaconine the two dominant glycoalkaloids, but several other glycoalkaloids may be found in wild species.

Solanine is a toxic bitter tasted glycoalkaloid (C45H73NO15). It is derived from the alkaloid solanidine with a carbohydrate side chain. It is distributed in leaves, fruits and tubers of potato and tomato. Its synthesis is considered as an adaptive defense strategy against herbivores. Intoxication (2-5mg/kg) from solanine leads to gastrointestinal issues like diarrhoea, vomiting, abdominal pain and neurological like hallucinations and headache. Similarly, it leads to poisonings in people with consuming berries from *S. nigrum*or *S. dulcamara*, or green potatoes.[12]

Extraction and purification of *Solanum* alkaloids

Extraction, purification, fractionation and identification of a bioactive compound from among a plethora of phytochemicals are nevertheless a simple procedure and it necessitates the requirement of having different approaches with respect to the nature of compound in interest. Overtime, many researchers formulated different methodologies for the effective isolation of alkaloids and later pharmacologists refined the protocols. Commonly employed alkaloid

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extraction processes include soxhlet, Stas otto process, Kippenberger's process, maceration, Manske's process, negative pressure cavitation extraction, pressurized solvent extraction, ultrasonic assisted extraction and pulse electric field extraction and for volatile alkaloids, steam distillation approach was used.[13] The alkaloids extracted by above mentioned techniques were likely to contain impurities and these can be removed by treating the extracted alkaloids with acid solution or precipitating alkaloids using precipitating reagents or crystallisation of alkaloid using suitable organic or mineral acid or by chromatographic technique (partition, column or ion-exchange).[14] Subsequently, the alkaloid mixture was fractionated by fractional distillation, fractional crystallization, derivatization or by various chromatographic techniques (HPTLC, HPLC, column or ion-exchange chromatography).[14] Individual alkaloids fractionated were then identified by NMR spectroscopy or X-ray crystallography.[15]

Table 4 Trade name of the alkaloids which are marketed as prescribed drugs

Diseases	Alkaloid	Product Name
Cancer	Vincristine Vinblastine Vinorelbine (semisynthetic) Taxol	Vincrisul™; Norcristine™ Periblastine™; Velban™ Navelbine® Taxol™
Lungs related disorders	Theobromine Theophylline Lobeline Ephedrine	Atrofed™ Theochron™ Lobatox™ Peripherin™
Muscle relaxant	Turbocuranine Galanthamine	Tubarine™ Nivalina™
Cough suppressant	Narceine Noscapine	Peneraj™ Bequitusin™
Anti-parkinson	Hyoscyamine Atropine	Cystospaz™; Donnatab™ Espasmo™;Protecor™
Analgesic	Codeine	Codicaps™;Tussipax™
Eye disorders	Strychnine	Dysurgal™

Table 5 List of Solanum alkaloids and its source

Alkaloid	Source
Solaverbascine	S. verbascifolium
Solanaviol	S. aviculare
Chaconine	S. tuberosum
Demissidine; Dihydrosolacongestidine	S. leucocarpum
Solanidane; Solanidine	S. tuberosum
Khasianine	S. xanthocarpum
Solangustine	S. angustifolium
Solacongestidine; Solafloridine; 23-oxo-solacongestidine; 24-oxo-solacongestidine	S. congestiflorum
15-alpha-hydroxy-soladulcidine; 15-alpha-hydroxy-tomatidine	S. dulcamara
Solamargine	S. palinacanthum; S. lycocarpum
Solamarine	S. dulcamara
Solanandaine	S. asperum
Solanigrine	S. nigrum
Solanine	S. nigrum; S. tuberosum
Solanocapsine; Solacasine; Solateinemine; 2-fluoro-2',4,5 benzenethanamine; hexatriacontane; 3-ethoxyamphetamine; 2,2,2-trichloroacetamide; O-methylsolanocapsine; Episolacapine; Isosolacapine	S. pseudocapsicum
Aculeamine	S. aculeatum
Solanopubamine	S. schimperianum
Solaparnaine	S. asperum
Solapalmitine; Solapalmitenine	S. tripartitum
Solaphyllidine; Desacetylsolaphyllidine	S. oblongifolium
25-isosolafloridine; Solacallinidine;	S. callium
Soladunalinidine	S. dunalianum
Solasodine	S. leucocarpum; S. trilobatum
Solasonine	S. lycocarpum; S. asperum
Solasurine	S. surattense
Solamine; Cuscohygrine; Anabasine	S. carolinense
Tomatidine	S. arboretum
Solasodamine	S. auriculatum; S. sodomaeum; S. marginatum
Solasuaveoline; Dihydrosolasuaveoline; Isosolasuaveoline	S. suaveolens
Tomatine	S. cathayanum
Solalyratines A and B	S. lyratum
Solamaladine	S. hypomalacophyllum
Solanocardinol	S. neocardenasii
Solanoforthine	S. seaforthianum
Solaradixine; Solashabanine; solaradinine	S. laciniatum
solaspiralidine	S. spirale
Solaverines	S. toxicarium S. verbascifolium
Solaquidine	S. pseudoquina

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Table 6 Derivatives of Solanum alkaloids and its therapeutic significance

Alkaloid	Derivative	Activity	Reference
Solanidine	solanidine N-oxide; 5 alpha, 6-dihydrosolanidine	Teratogenicity	42
Solasodine	solasodine O-(diethyl phosphate); N-acetyltetrahydrosolasodine	Cholinergic	85,86
Tomatidine	Dihydrotomatidine; Pregnane derivative	toxicity study; neuritogenic and ngf-enhancing activities.	87,88
Solamargine	(25R)-3b-{O-a-L-rhamnopyranosyl-(1®2)-[O-a-L-rhamnopyranosyl-(1®4)]-b-D-glucopyranosyloxy}-22a-N-spirosol-5-ene	Anticancer	89
Solanopubamine	3-βN, 23-βO-diacetylsolanopubamine; 3, 3-βN,βN-dimethyl-βO-methylsolanopubamine; 3-βN-octadecanoly-solanopubamine; solanopubamine-23-βO-octadecanoate; Solanopubamine 23-βO-undec-11-enoate; Solanopubamine-23-βO-acetate	Anticancer and antimicrobial	42
Chaconine	6-O-sulfated chaconine	Cytotoxicity studies	90
Solanine	6-O-sulfated solanine	Cytotoxicity studies	90

Extraction protocols of alkaloids from *Solanum* species have been proposed by many researchers. Tomatine, solasonine and solamargine were considered to be the most common *Solanum* alkaloids. Guo et al.,[16] employed aqueous extraction protocol for isolating solasonine and solamargine from *S. nigrum*, whereas alpha-tomatine was purified by infusion-extraction method from the leaves of *Solanum lycopersicum*.[17] Bhattacharya et al.,[18] isolated crystalline solasodine from the fruit of *Solanum xanthocarpum*. Solanaviol, relatively a rare *Solanum* alkaloid was extracted by Laskin et al.,[19] Pressurized liquid extraction of solanidine from potato peels was described by Hossain et al.,[20]

Biological potentialities of *Solanum* alkaloids

Solanum species are traditionally used for curing many disorders including antimetastasis. Over time many workers have attempted to scientifically validate this traditional knowledge. Some worked on the crude plant extracts while others isolated the typical phytochemical like alkaloids and polyphenols and some fractionated the active principle or the potent derivatives (Table 6). Biological activities of *Solanum* alkaloids and its derivatives are carried out including their genes regulating their biosynthesis.

Anticancer activities

In India, cancer has been identified as one of the leading causes of mortality with a frequency rate of 0.4million deaths per year. Moreover, a drastic increase has been recorded year after year.[21] However, in most cases conventional radiotherapy or chemotherapy approach was considered for the treatment. But the drug resistance gradually developed by the patient was found to be a major hurdle in the treatment of cancer by chemotherapy. Thus, there is an increased demand for formulating more potent novel drugs or that complement the existing ones. In this juncture, alkaloids isolated from *Solanum* species were attempted as the anticancer agents.

Alpha-chaconine, a derivative of the aglycone solanidine, exhibited remarkable inhibition of proliferation, invasion and migration of A549 cells (lung adenocarcinoma cell) as well as bovine aortic endothelial cells (BAECs). The underlying molecular mechanism of these antimetastatic activities was shown as inhibition of phosphorylation of JNK and Akt pathways. However, the alkaloid has no effect on the phosphorylation of ERK and p38. Further, alpha-chaconine remarkably lowered the nuclear level of NF-kappaB factors and expression of matrix metalloproteinase-2/-9 (MMP-2/-9) in A549 cells and MMP-2 in BAECs (matrix metalloproteinase-2 is involved in angiogenesis).[22,23] Reddivari et al.,[24] reported that a combination treatment of gallic acid and alpha-chaconine was effective against the proliferation of prostate cancer cells lines such as LNCaP and PC-3. Interestingly the same combination triggered caspase-dependent apoptosis in LNCaP cells and increased cyclin-dependent kinase inhibitor p27 levels in LNCaP and PC-3 cell lines. This apoptotic effect can be attributed to activation of JNK produced by the combined effect of alpha-chaconine and gallic acid.

In cancer studies, solanine exhibited promising chemoprotective and chemotherapeutic effects via induction of apoptosis, inhibition of proliferation, migration, invasion and angiogenesis. In *in vitro* and *in vivo* studies of alpha-solanine significantly inhibited proliferation of human pancreatic carcinoma cell lines (PANC-1, SW1990, MIA PaCa-2 cells), human melanoma cell line (A2058), human prostate cancer cell (PC-3) and mouse mammary carcinoma cells. Solanine treated mouse exhibited an increased expression of proapoptotic Bax protein. The suppression in expression of antiapoptotic Bcl-2 protein and angiogenic parameters in solanine-treated mouse were reported. Further, suppression of phosphorylation of Akt, mTOR, and Stat3, strengthened phosphorylation of β-catenin and decreased expression profile for β-catenin and TCF-1 were documented for PANC-1 cells following solanine treatment. α-solanine inhibited NF-κB activity in PANC-1 and A2058 cell lines and also inhibited JNK in A2058 cells and PI3K/Akt signaling pathways in A2058 and PC-3 cells. Alpha-solanine elevated the expression of E-cadherin in PANC-1 and human prostate cancer cell (PC-3), correlated with reduced mRNA level of matrix metalloproteinase (MMP-2/9) and extracellular inducer of matrix metalloproteinase (EMMPRIN) in PANC-1 and PC-3 cell lines. Suppression of ERK, down regulation of oncogenic microRNA-21 (miR-21) and up regulation of tumor suppressor miR-138 expression was noted in solanine treated PC-3 cells. These research findings proves significant therapeutic potentiality of α-solanine in inhibiting proliferation and suppressing the invasion of various carcinoma cells.[25,26]

Solanidine another alkaloid, exhibited suppression of proliferation of MCF-7 cancer cell lines under *in vivo* conditions.[27] Inhibition of proliferation of human leukemia cells (HL-60) by chemically

Citation: Jayakumar K, Murugan K. *Solanum* alkaloids and their pharmaceutical roles: a review. *J Anal Pharm Res.* 2016;3(6):397–408.
DOI: 10.15406/japlr.2016.03.00075

synthesized three solanidine analogues were evaluated in yet another study. Interestingly data revealed a similar cytostatic effect for all the three analogs, with an IC50 value range of 1.27-2.94. Similarly, increase in condensation of chromatin materials and membrane permeability was also observed (Hoechst staining method). In continuation, delayed G1, S and G2/M phases were noticed within a span of 24h. A gradual reversal in these activities also noted after 48h (flow cytometry). Another solanidine analogue demonstrated inhibitory properties towards ribonucleotide reductase and bear significant free radical scavenging activity.[28] Study on solanidine effect on human 1547 osteosarcoma cells, revealed significance of conformation at C-5 and C-25 carbon atoms, hetero-sugar moiety and the 5,6-double bonds in inducing apoptosis and favouring cell cycle arrest.[29] Despite of having desirable antiproliferative effect against cancer cells, this compound was reported to have high retention period in human body. Study on the absorption and retention of solanidine in the human body revealed an increase in solaniine level in RBC compared to that of plasma, with poor excretion rate through urine and stool. Further, spectroscopic studies of solanidine from human liver, proposed prolonged storage of solanidine may lead to undesired effects and metabolic stress.[30]

Several studies examined the effect of tomatidine on the migration and invasion of cancer cells. Anticancer effect of alpha-tomatine was confirmed by Tomsik et al.,[31] against solid Ehrlich tumour in mice. *In vitro* analysis of human lung adenocarcinoma A549 cells with tomatidine resulted in significant suppression of cell invasion (Boyden chamber invasion assay) but does not exhibited effective inhibition of migration and viability of A549 cells. Furthermore, tomatidine reduced MMP-2 and MMP-9 (matrix metalloproteinase-2/-9) mRNA level, extracellular signal regulating kinase (immunoblotting assays), phosphorylation of Akt, nuclear level of NF-κB and increased the expression of tissue inhibitor of metalloproteinase-1 (TIMP-1). These findings suggest the possible utilization of tomatidine as a potent therapeutic drug in anti-metastatic therapy.[32] α-tomatine when administered with paclitaxel (standard drug for cancer), exhibited enhanced apoptosis of PC-3 cells (by PI3K/Akt inhibition, elevated BAD and lowered Bcl-2 and Bcl-xL expression) and reduced cell viability. However, this combination produced no inhibition of RWPE-1 (non-neoplastic prostate), but very effectively controlled subcutaneous tumor development in mouse. These findings propose that alpha-tomatine can be an effective drug in combination with paclitaxel against prostate cancer.[33]

Further, solamargine significantly lowered cell viability and induced apoptosis in SMMC-7721, HepG2 cells, multi drug resistant K562/A02 cells and osteosarcoma U2OS cells. Solamargine increased the mRNA, protein expression of p53, Bax and Bcl-2 in U2OS and K562/A02 cells (real time-PCR, western blot), whereas a suppression in phosphorylation of Akt, mRNA expression and promoter activity of EP4, protein expression of SP1 and NF-κB subunit p65 were noted in lung cancer cell lines. A down regulation of MDR1 mRNA, P-glycoprotein and actin were noted in solamargine treated K562/A02 cells. Further, solamargine enhanced cytochrome c release and up regulation of caspase-9 and capsase-3 in U2OS, SMMC-7721 and HepG2 cells (western blot, colorimetric assay). In SMMC-7721 and HepG2 cells, solamargine caused cell cycle arrest at phase G2/M.[34,35] Most of the researchers also correlated the role of carbohydrate moiety of solamargine in inducing apoptosis.

Anticancer properties of solasodine in mice model was attempted and found that under *in vivo* solasodine glycosides treatments exerted significant inhibition of murine sarcoma 180 cell lines (S180).[36] Based on further molecular investigation, the probable role of rhamnose in solasodine glycosides binding on tumour cells and its specificity was proposed. 0.005% mixture of solasodine glycosides (Zycure) was demonstrated to be an effective dose on human beings. 0.005% exhibited 66% and 78% curability at 56days and 1year follow-up, respectively.[37] In another study, the importance of carbohydrate moiety (C3 side chain) and conformation at C-5 and C-25 of solasodine in apoptosis induction was evaluated. Further, cell toxicity, cell proliferation inhibition, cell cycle arrest and induction of apoptosis (human 1547 osteosarcoma, MCF-7) was also evaluated by many workers.[38]

Khasianine is a steroidal alkaloid. Khasianine C3 side chain possess 4'Rha-Glc. The cytotoxic studies on human hepatoma cells showed that this alkaloid has an insignificant toxic effect against cancer cells. Carbohydrate moiety in khasianine has a regulatory effect on expression of TNFR I and II. These results propose that the carbohydrate moieties seen in steroidal alkaloids may have a role in altering the binding specificity to steroid receptors which ultimately result in gene expression regulation in varied manner.[38] Akter et al.,[38] worked on cell cycle arrest and anti-apoptotic properties of khasianine on MCF-7 cell lines. Several studies evaluated cytotoxicity of O-methyl solanocapsine against various malignant cell lines such as Vero, HeLa, HEp-2 and A-549 cell by SRB and MTT methods. HeLa cell culture found to be more susceptible to O-methyl solanocapsine.[39]

Steroidal alkaloid soladulcidine isolated from *Solanum dulcamara* and ten of its derivatives were shown to have significant antiproliferative effect against prostate cancer (PC-3) cells. Further, compound designated 19 in the series showed the highest suppression of PC-3 cell proliferation with an IC_{50} value of 4.8±0.9μmol/L.[40] Beta-solamarine from *Solanum dulcamara* has been hypothesised to bear tumor-inhibitory activity against Sarcoma 180 in mice.[41] Al-Rehaily et al.,[42] evaluated cell toxicity of solanopubamine and its derivatives against various cancer cell lines. Solanopubamine alone exhibited remarkable inhibitory action against many tumor cell lines. Solasonine from *Solanum lycocarpum* fruit was evaluated for the inhibition on various tumor cell proliferations. Among the various cell lines evaluated such as B16F10, HT29, MCF-7, HeLa, HepG2, MO59J, U343 and U251 by MTT assay, HepG2 was found to be most susceptible with IC_{50} 6.01μg/mL.[43]

Neurotoxicity and neuroprotective activity

Neurotoxicity refers to structural or functional damage occurred to nervous system caused by agents which usually result into impaired or altered functioning. Impairment in function may occur via interactions of toxic agents with the normal neurotransmission mechanisms with or without causing structural damage. Expression of these effects is sometimes spontaneous or transient and still others are much more insidious. The search for novel molecules that can interact with central nervous system (CNS) and can be used for treatment purposes was initiated in the nineteenth century. However, investigations targeting plant sources with this sort of biological activity was limited. Many of the *Solanum* alkaloids are shown to have regulatory activity on nervous system at low dosage regimens, but exert its neurotoxicity above optimal doses.

Neuroprotective activity of solasodine was evaluated against ischemia in rats. The suppression of LPO and NO and enhancement of GSH, CAT and thiols was observed in ischemic rats after solasodine administration. Also solasodine exhibited neuron protection in brain coronal region as revealed by histopathology studies. Based on these findings, a part of protective activity of neuron exhibited by solasodine could be ascribed by its free radical scavenging properties.[44] In addition to neuroprotection, solasodine was experimentally showed to possess

significant neurogenesis properties in mice model. Solasodine induced differentiation of mouse embryonic teratocarcinoma P19 cells into cholinergic neurons with axonal formation. Also, solasodine treated left brain ventricle exhibited remarkable hike in bromodeoxyuridine utilization by ependymal cells. Moreover, differentiated and matured ependymal cells regained their division and differentiation properties. Solasodine stimulated GAP-43/HuD signal pathway and regeneration of neuroblasts and GABAergic progenitors in GAD65-GFP mice.[45]

Neuroprotective effects of tamatidine has been demonstrated by Taveira et al.,[46] Tamatidine exhibited protective effect on neuron against glutamate-induced cell toxicity in SH-SY5Y neuroblastoma cells. Further, tomatidine was shown to have interacted specifically with alpha 7 type nicotinic receptors, there being nullifying its effect on muscarinic receptors. Thus, the selective cholinesterases inhibition of tomatidine eventually may find its way in the development of novel neuroprotective drugs.

Rozengart et al.,[47] conducted a comparative study on the effect of 18 different anabasine derivatives, on the activity of brain cholinesterase and visual ganglia of *Rana temporaria* (frog) and squids (*Todarodes pacificus* and *Berryte uthis*). Its effect on butyrylcholinesterase (serum) and acetylcholinesterase (erythrocyte) was also determined.

O-alkyl-O-(anabasinoisopropyl)- and O-alkyl-O-(anabasinobutin-2-yl)-phenylphosphonates and diphenylphosphynates has been evaluated for its anti-monooxygenase and anti-cholinesterase potentialities. Anticholinesterase property of these compounds were found to be dependent upon the structure of phosphoryl part and alkyl radical of the investigated molecule. Further, antimonooxygenase test, showed that these compounds were better inhibitors than the standard inhibitor SKF.[48]

Roddick et al.,[49] showed that up to a range of 100μM, β-solamarine has no influence against acetylcholinesterase but at higher doses it cause membrane damage. Garcia et al.,[50] proved the possibility of the synthesis of ideal acetylcholinesterase inhibitor from solanocapsine and its synthetic derivatives, as a probable cure for Alzheimer's disease.

Similarly, direct excitation of cholinergic receptors may be another possible way for neutralizing scopolamine related amnesia when compared with indirect excitation of cholinergic receptors by inhibitors of cholinesterase. Further, scopolamine is playing variable roles in ambulation, grooming and rearing responses. For example at higher dose of scopolamine leads to an increase in rearing and U shaped response curve for ambulation, there being producing nil effect on grooming. Pine needle extract counteract the effect of scopolamine induced memory impairment (amnesia) in mice. Experimentation of mice pre-treated with pine extract followed by scopolamine injection intraperitoneally to evaluate the memory function test by Morris water maze task method exhibited a rise in cumulative path-length, escapes latency and lessened time spent in target quadrant. Further, pre-exposure to pine needle extract significantly counteracted the scopolamine induced impaired acetylcholinesterase and neurogenesis function and also improved multiplication and maturation of neurons.[51]

Antimicrobial, aphicidal, trypanocidal, molluscicidal, schistosomicidal, leishmanicidal potentialities

The purified alkaloid demissidine along with the alkaloids tomatidine, dihydrosolacongestidine and solasodine from *Solanum leucocarpum* were showed bactericidal activities.[52] Similarly, antibacterial properties of solacasine from *S. pseudocapsicumhave already been reported*.[53] Fungicidal potentiality of the alkaloid solacongestidine against selected fungal strains such as *Candida albicans*, *Cryptococcus albidus* and *Trichophyton rubrum* revealed significant MIC values and time kill analysis.[54] Moreira *et al*.,[55] investigated trypanocidal activity of solamargine isolated from the fruits of *S. palinacanthum* and *S. lycocarpum* by MTT colorimetric assay. In *in vitro* studies, solamarine exhibited strong molluscicidal properties against snail, *Galba truncatula*.[56] Solanopubamine exhibited remarkable fungicidal activity against *Candida albicans* and *C. tenuis*.[42] Solaphyllidine and desacetylsolaphyllidine from *Solanum oblongifolium*, were studied for their effects on pathogenic microbes.[57] Solasodine from *S. leucocarpum* showed inhibitory action against *Staphylococcus aureus* in agar well diffusion assay.[52] Some other works studied the antifungal properties of solasonine against *Rhizoctonia solani* and *Phoma medicaginis* over a wide range of pH. However, solasonine showed no action against *Rhizoctonia solani*, but significantly inhibited mycelia growth of *P. medicaginis* in a pH dependent manner. Inhibitory activity increased with an increase in pH (as indicated by dose-response curves). Interestingly, a combination of solasonine and solamargine in the ratio 1:1 produced more potential inhibition (50μM each) and found to be effective against *R. solani*, but not influenced by pH.[58]

Tomatidine, an aglycone of tomatine, possess strong antimicrobial effects. *Staphylococcus aureus*, is considered to be one of the noxious infectious agent due to its resistances to many of the available synthetic antibiotic drugs. *S. aureus* has the ability to produce small-colony variants (SCVs) with reduced susceptibility to aminoglycoside antibiotics. Studies has shown that tamatidine possess significant inhibitory effect against small-colony variants growth. The underlying mechanism of bactericidal activity was attributed by the impaired or dysfunctional electron transport system caused by tomatidine treatment in *S. aureus* cells. Further, tomatidine blocks the intracellular replication of a clinical SCV in polarized CF-like epithelial cells. These results indicate that the alkaloid tomatidine may be used as microbicidal either alone or in combination therapy with traditional antibiotics to eliminate resistant strains of *S. aureus*.[59]

Solasonine (50μM) in *in vitro* conditions exhibited schistosomicidal properties against *Schistosoma mansoni*. Schistosomicidal properties include tegument damage and suppressed egg development. When supplemented in combination with solamargine, an augmentation in these results was noted. In another study solasonine exhibited leishmanicidal activity against *Leishmania amazonensis* (protozoa). Here also an equimolar mixture of solasonine and solamargine, exhibited better activity.[60] Further, solasonine and solanandaine from unripe *S. asperum* fruits was validated for its molluscicidal activity against *Biomphalaria glabrata*.[61]

Anabasine, an alkaloid showing close proximity to nicotine and was validated for its antimicrobial (antibacterial and antifungal) efficacy. Kulakov et al.,[62] synthesised thiourea derivatives of anabasine and evaluated its antifungal and antibacterial properties. Parallely, Bakbardina et al.,[63] chemically synthesised alkaloid anabasine and cytisine derivatives of monothiooxamides and determined its biological activity in terms of aphicidal and fungicidal properties. Anabasine showed strong insecticidal properties against Lepidopterous larvae (*Pieris rapae* larval bioassay). Use of anabasine even in trace amounts in insect traps proved to be effective in killing insects.[64] Solaverbascine, a new alkaloid from *S. verbascifolium*, displayed significant germicidal properties.[65]

Anti inflammatory effects

Chronic inflammation is an undesirable phenomenon and gets aggravated with the chronic diseases such as cancer, autoimmune

disorders, arthritis and vascular disorders. Numerous studies have proved that natural compounds or extracts as human health rejuvenators with safety and non-toxic effects. Eventhough many of the phytochemicals isolated from herbs have exhibited anti-inflammatory effects, only a few studies have investigated the underlying molecular events in anti-inflammatory actions of phytochemicals.

Solanidine, α-chaconine and α-solanine were reported as anti-inflammatory compounds. Kenny et al.,[66] revealed that α-chaconine and solanidine exhibited significant inhibitory action on the production of key inflammatory compounds such as interleukin-2/8 in Con A-induced Jurkat cells. Further, nitric oxide production was significantly reduced in LPS-stimulated raw macrophages following α-solanine and solanidine treatment. Pandurangan et al.,[67] evaluated anti-inflamatory activity of solasodine from *S. trilobatum* in animal models. Solasodine exerted antiinflammatory effect in a concentration dependent manner in carrageenan-induced rat paw oedema. Interestingly, solasodine on topical application significantly reduced tetradecanoyl-phorbol 13-acetate induced inflammation in ear. Further, reduction in exudates volume, leucocyte count as well as neutrophil migration was recorded following solasodine administration. Zhao et al.,[68] demonstrated that α-tomatine also showed similar effects. Expression of pro-inflammatory cytokines was greatly suppressed by α-tomatine in LPS (lipopolysaccharide) induced macrophages. Chiu et al.,[69] compared *Solanum* alkaloids specially tomatidine and solasodine against LPS-stimulated inflammation in macrophage. Tomatidine found to be more effective in suppressing inflammation than solasodine by attenuating the expression of NF-κB and JNK signalling molecules.

Antioxidant potential/degenerative disorders and anti-aging

Uncontrolled synthesis of free radicals or ROSs results into many neurodegenerative disorders can trigger aging and can be regulated by exogenous antioxidants. Extracts of *Solanum* specieshave shown potential antioxidant power in 1, 1-diphenyl-2-picryl hydrazyl (DPPH) radical scavenging, ABTS, FRAP, O2.-, H2O2 etc. Positive correlation was noticed between the antioxidant activity and the content of alkaloids, signifying that the compounds to the radical scavenging potentiality. But the mechanism of scavenging action by stimulating cytokines (interleukin IL -2, IL-4, IL-12, IFN-g and tumor necrosis factor-alpha TNF-g) remains to be elucidated.[70]

Toxicity studies

Administration of α-solanine (75-100mg/kg body weight) on a daily basis found to be lethal in hamsters within 4-5days. Solanine treated animals were also suffered from other undesired effects such as fluid-filled and dilated small intestines. α-solanine induced craniofacial malformations (exencephaly, anophthalmia and encephalocele) on oral administration in Syrian hamsters. These toxic effects of solanine were attributed by the ionic imbalance in the cells. Several studies investigated the effects of solanine on intracellular concentration of Ca^{2+} on mouse neuroblastoma x rat glioma hybrid NG 108-15 cells, mouse-skin fibroblastoma L-929 cells and mouse Balb/3T3 cells lines. The results revealed that the solanine-evoked Ca^{2+} influx due to the destabilization of the cell membrane. Further, all the solanine treated cell lines showed a marked increase in intracellular Ca^{2+} concentrations with the concentration of solanine.[71]

In one investigation, solasodine produced sterility in male rats and dogs. The effect was reversed on cessation of solasodine supplement. Further testing showed inhibition of spermatogenesis and testosterone production and reduced movement of sperm in solasodine treated groups, without any remarkable change in size of sex organs.[72] Above optimal doses anabasine is believed to be teratogenic in swine.[73]

Jacob et al.,[74] studied 304 individuals (205 individuals used smokeless tobacco and 99 were cigarette smokers) showed that presence of anabasine in urine samples and can be used as an effective marker to validate tobacco abstinence or to measure the extent of use of tobacco in individuals who undergo nicotine replacement therapy.[74] von Weymarn et al.,[75] developed a 96 well plate-based capillary LC-tandem mass spectrometry method which was regarded to be accurate and precise for the analysis of anabasine and two more compounds nornicotine and anatabine in urine. Study was carried out on 827 smokers with a vast range of tobacco exposures. Traces of anabasine were found in almost all the sample of urines (97.7%). The average amount of anabasine in urine was detected as 5.53ng/mL. The median ratio of the glucuronidated to free anatabine was 0.74 (range, 0.1 to 10.9), and the median ratio of glucuronidated to free anabasine was 0.3 (range, 0.1 to 2.9).[75]

Locomotor activity

Locomotor activity in scopolamine treated mice strains, namely A, DBA/2 and C57BL/6, in association with shock treatment revealed behavioural suppression.[76] Another study in rats, demonstrated the effects of scopolamine on pre and post-synaptic events related with dopaminergic function. Scopolamine showed antagonist effects against inhibition produced by spiperone on apomorphine associated behavioural action. In animals, exposed to 6-hydroxydopamine (6-OHDA), an increase in scopolamine-induced locomotor activity was noted, but α-methyltyrosine inhibited this stimulation. However, the enzyme dopamine-beta-hydroxylase remains unaffected in these treatments supports the hypothesis that scopolamine association with presynaptic dopaminergic fibers. Also, when alpha-methyltyrosine was administered to rats with 6-OHDA, recorded a suppression of spiperone inhibition of locomotion induced by apomorphine. In addition, the level of 3H-spiperone in brain and dopamine associated activity of adenylate cyclase remains unchanged confirming the post-synaptic association of scopolamine.[77] Solaphyllidine and desacetylsolaphyllidine from *S. oblongifolium*,were studied for their effects on locomotor activity (mice) i.e., both the alkaloids reduced duration of sleep, while, solaphyllidine enhanced locomotor activity.[57]

Action on cell membrane

The effects tomatine on membrane damage was assessed by measuring intracellular free Ca^{2+} level in NG 108-15 cells, L-929 cells and Balb/3T3 cells in rat model. Positive correlation was seen with the concentration of tomatine with intracellular Ca^{2+} level i.e., remarkable ED_{50} in NG 108-15 cells was noticed. These findings suggest the role of tomatine in membrane damage or in combination with other alkaloids associated poisoning.[78] A similar trend was also noticed with α- chaconine. The Ca^{2+} influx evoked by α-chaconine could not be prevented by metal ions or by inhibitors of Ca^{2+} transport across membranes such as voltage-operated channel antagonists, muscarinic and nicotinic antagonists or Na(+) and K(+) channel blockers. The optimal concentrations of alpha-chaconine that yield half-maximal response (ED_{50}) in NG 108-15 cells, L-929 and Balb/3T3 were 12.0 mum, 10.2 mum and 9.5 mum respectively. The result supports the assumption that the alkaloid-evoked Ca^{2+} influx may be due to the cell membrane destabilization. Chaconine was also assayed by Roddick et al.,[49] in order to assess its effect on disruption of cell membrane and enzyme-inhibition.

Hepatoprotective activity

Hepatomegalyic (liver weight increase) effect of tomatidine was evaluated by Friedman et al.,[79] Pregnant and non-pregnant mice were fed with 2.4 =mmol/kg of tomatidine for 14days. The ratios of liver weight to body weight % in non-pregnant mice, were found to be markedly higher than those of the control values with a propotional increase in pregnant mice. Further, in this study tomatidine exerted insignificant effects on the weight of the foetuses in pregnant mice and also no abortion of foetuses were reported. In another study, khasianine remarkably suppressed CCl4 induced liver damage under *in vitro* condition.[80]

Effect on cholesterol

Fujiwara et al.,[81] examined the inhibitory effects of tomatidine on the accumulation of cholesterol ester (CE) in human monocyte-derived macrophages (HMDM) and also atherogenesis in mice with apoE-deficiency. Tomatidine showed a concentration dependent suppression of cholesterol ester accumulation induced by acetylated LDL in HMDM. In Chinese hamster ovary cells, CE formation found to be greatly suppressed after tomatidine treatment. Further, tomatidine suppressed the ACAT-1 and ACAT-2 activities (cholesterol acyl-transferase-1/-2) in hamster ovary cells. Tomitidine, on oral administration to mice with deficiency in apoE, significantly lowered levels of LDL-cholesterol, serum cholesterol and areas of atherosclerotic lesions. These results indicate the significant potentiality of tomatidine in suppressing ACAT activity and inhibition of atherogenesis.

Other activities

The alkaloids demissidine along with other alkaloids tomatidine, dihydrosolacongestidine and solasodine purified from *S. leucocarpum* were evaluated for their effects on topoisomerase I and II activities in mutant yeast.[52]

Beta-solamarine, solamargine and chaconine in *in vitro* studies exhibited haemolytic properties against RBC. Roddick et al.,[49] studied membrane damage and enzyme activity inhibition of solasonine. As the study reveals that a combined application of solasonine and N-nitrososolamargine failed to produce any liposomes disintegration. But with 75µM solamarine, solanine and solatriosides, solasonine produced disruption of liposome and also exhibited disruption of erythrocytes.

Genes regulating alkaloid synthesis in *Solanum*

Most of the *Solanum* members are toxic because of certain metabolites like glycoalkaloids. Many workers attempted to elucidate gene regulated biosynthetic pathway related to glycoalkaloid synthesis particularly in potato. Nurun[82] reported six genes in association with steroidal glycoalkaloids (SGA) and sterol biosynthesis in potato. Down regulation of StDWF1 (gene encoding a sterol Δ 24-reductase) reduced both cholesterol and steroidal glycoalkaloid content (SGA), suggesting some crosstalk between sterol and SGA synthesis. Carpintero et al.,[83] studied expression of genes related to steroidal glycoalkaloid (SGA) metabolic pathway, namely HMG1 (3-hydroxy-3-methylglutaryl coenzyme-A reductase), HMG2, SQE (squalene epoxidase), SGT1 (solanidine galactosyltransferase) and SGT2 (solanidine glucosyltransferase).[83] Similarly, Mariot et al.,[84] based on genetic analysis in *S. tuberosum* proposed existence of relationship between content of total glycoalkaloid (TGA) and the expression profile ofSGT1, SGT3 and GAME genes in S. tuberosum.[85–90]

Conclusion

Solanum species are unique source of several pharmacologically important lead molecules, especially steroidal alkaloids such as solasodine, solasonine, solamargine and various other medicinally useful alkaloids. This review has attempted to bring almost all sort of scientific information in relation to pharmacological studies conducted on *Solanum* alkaloids. As most of the studies are basic and are not up to the quality for the synthesis of compounds with prescription grade, this comprehensive review is expected to help the investigators to explore deep into this field that may benefit the development and emergence of new molecules with significant therapeutic activities.

Acknowledgments

None.

Conflicts of interest

Author declares there are no conflicts of interest.

Funding

None.

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Citation: Jayakumar K, Murugan K. *Solanum* alkaloids and their pharmaceutical roles: a review. *J Anal Pharm Res.* 2016;3(6):397–408.
DOI: 10.15406/japlr.2016.03.00075