

Review Article

## ROLE PLAY OF HERBAL INGREDIENTS IN THE WORLDWIDE AILMENT OF DIABETES MELLITUS

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### ABSTRACT

Diabetes Mellitus is one of the major endocrine disorders affecting nearly 10% of the worldwide population and now a days it's becoming a key issue for concern. In this review article, we studied the hypoglycemic activity of different medicinal drugs. We mainly focused on the four medicinal plants i.e: - *Gymnena Sylvestre*, *Salacia Reticulata*, *Swertia Chirata*, *Pterocarpus Marsupiam*. In this the active constituents which we observed for the hypoglycemic activity were Gymnemic acid, Mangiferin, Kotalanol, Salacinol, Swertiamarin, Amarogentin, Liquiritigenin. These phytochemical constituents behaved as antidiabetic agents due to the interaction with multiple targets including alpha glucosidase, GADPH, Sodium symporters, PPAR-g expression, analyse.

### 1. INTRODUCTION

In the recent scenario, everyone must have come across certain diseases associated to our lifestyle or other medical issues. The most common ones that have invaded almost in every other family includes diabetes, obesity, hypertension, etc. Herbal medicine, phytomedicine or botanical medicine are synonymous which uses plants for medicinal purposes. Therapeutic utilization of natural medication in the treatment and anticipation of disease including diabetes has a long history contrasted with conventional medication. [1] According to “9th edition of International Diabetes Federation (IDF) Atlas”, diabetes is one of the fastest growing global health emergencies of 21st century. As per the data 2019,463 million people were estimated to have diabetes and the data was projected to reach 578 million by 2030 and 700 million by 2045. [2]. Diabetes mellitus is a metabolic disorder that influences the body's capacity to make or utilize

insulin. Insulin is a protein hormone which is produced by the pancreas that regulates the metabolism of glucose, fat, and protein in the body. Diabetes results in abnormal levels of glucose in the circulation system. [3,4]

Conventionally, medicinal plants were an indispensable element for the public health management. About 35% of the population still rely on herbal medical care. This count is increasing lately as the diversity of medicinal plants is evidently beneficial in healthcare field. [5]. Today, many of the anti-diabetic treatments includes the use of medicinal plants. Most plants contain carotenoids, flavonoids, terpenoids, alkaloids, glycosides that often have anti-diabetic effects. The main purpose of this article is to introduce a number of effective medicinal plants which is used as anti-hyperglycaemic drugs along with the mechanisms of plant compounds which is used to reduce glucose levels and increase insulin secretion. [6] In this article we will discuss Gymnemic

acid, *Salacia Reticulata*, *Salacia chinensis*, *Swertica Chirata*, *Pterocarpus marsupium* These are few herbal drugs which have antidiabetic effect. Also, herbal drugs are now becoming common in use due to the following reasons as Permanent Cure, less adverse effect, safe, cheap and eco-friendly.

## 2. GYMNENA SYLVESTRE

The one of the most potential medicinal plants is *Gymnena Sylvestre*, which belongs to the family of Apocynaceae. It is a wild herb located in India, Africa, Australia, and China. It is a woody plant, climbing vine with ovate and elliptic leaves and it have a bell shape yellow flowers. The word “Gymnema” is derived from a Hindi word “Gurmar” meaning “destroyer of sugar” and it also have a sugar lowering property. So, it’s most common name is Gurmar. It is known as Meshashringi, Merasingi, Kavali, Kalikardori, Vakundi, Dhuleti, Mardashingi, Podapatri, Adigam, Cherukurinja, Sannagerashambu, Chigengteng or Australian Cowplant, Waldschlinge in German, *Periploca* of the

woods in English. *Gymnena Sylvestre* was considered as one of the major botanicals and a traditional therapy to treat diabetes in the Ayurvedic system of medicine and also is included in Indian Pharmacopoeia as an anti-diabetic plant. [7-9].

### 2.1. Active Constituents

The main constituent of *Gymnena Sylvestre* is found to be gymnemic acid, a mixture of about 17 different saponins. This acid that is commonly used as a marker for standardization and quality control in many commercial preparations of gymnema. Also, many other chemical constituents have also been found in *G. sylvestre*, for example- gymnemasaponins- it is another major component of gymnema, of which there are at least seven different types. These constituents, as well as the polypeptide Gurmarin, the alkaloid conduritol, gymnamine, gypenoside, and the dammarane-type saponins gymnemasides 1–5 and gymnemasin B, C, and D are all likely to be responsible for the antidiabetic property and antisaccharin effect of the plant. [10]

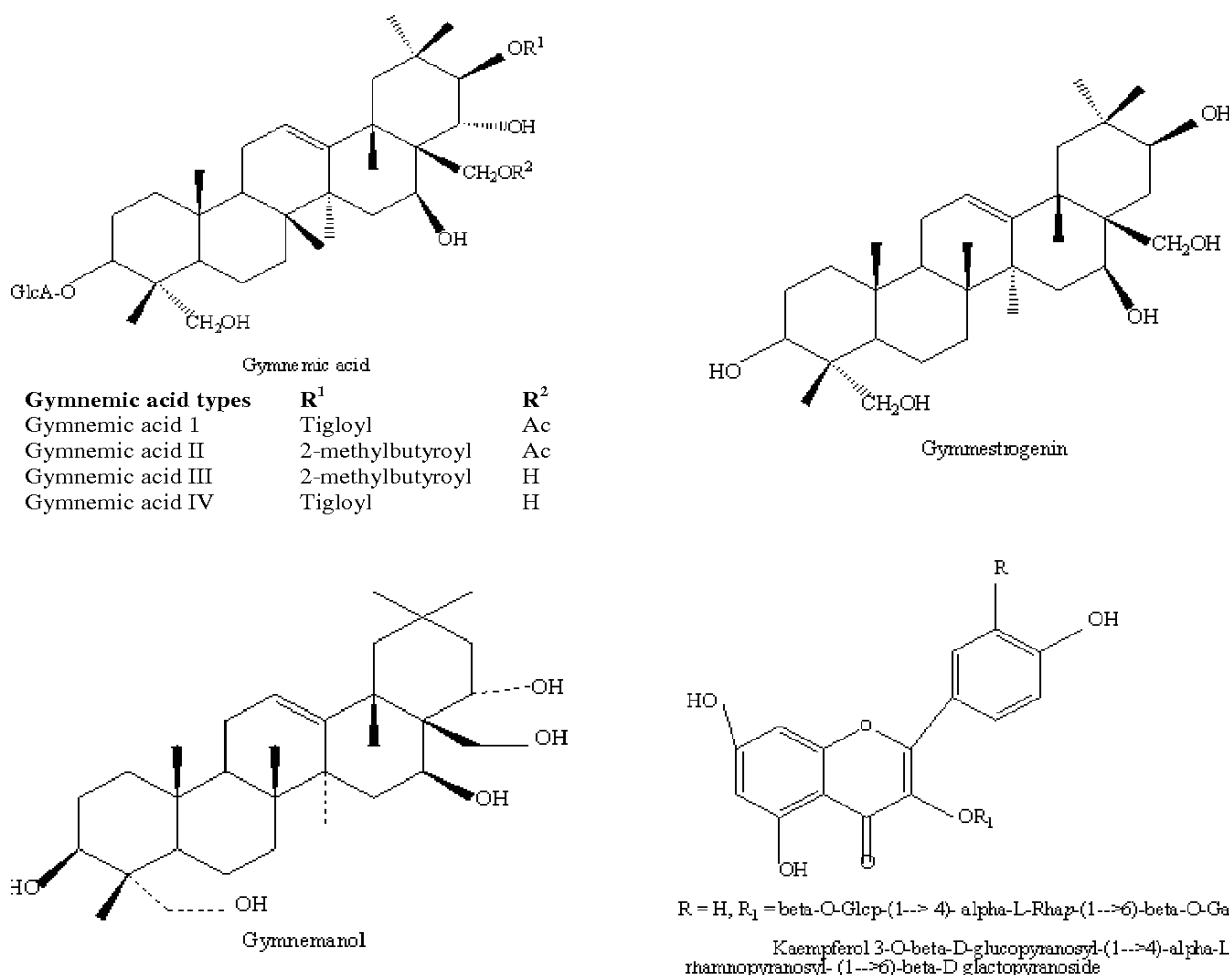


Figure 1 Structure of some phytoconstituents isolated from *Gymnena Sylvestre* [11]

### 2.2. Mechanism of Action

*G. Sylvester* leaves have been found to produce anti-diabetic effect in laboratory animals and delay glucose absorption from the intestine into the blood and hence use to treat hyperglycemia.

There are some possible mechanisms by which the leaves extract of *G. Sylvestre* possess its hypoglycaemic acid effects are:

- It enhances the regeneration of islet cells,
- It enhances the secretion of insulin,
- It causes inhibition of glucose absorption from intestine,

It enhances the use of glucose by the body, as it increases the activities of enzymes responsible for utilization of glucose by insulin-dependent pathways, an increase in phosphorylase activity, decrease in gluconeogenic enzymes and sorbitol dehydrogenase. Gymnemic acid molecules also bind to the receptors (Na<sup>+</sup>-glucose symporter) which is located in the intestine, thereby halt the absorption of glucose. [12,13,14]. The mechanism of *Gymnema Sylvestre* is also explained in flow chart shown in figure 1.

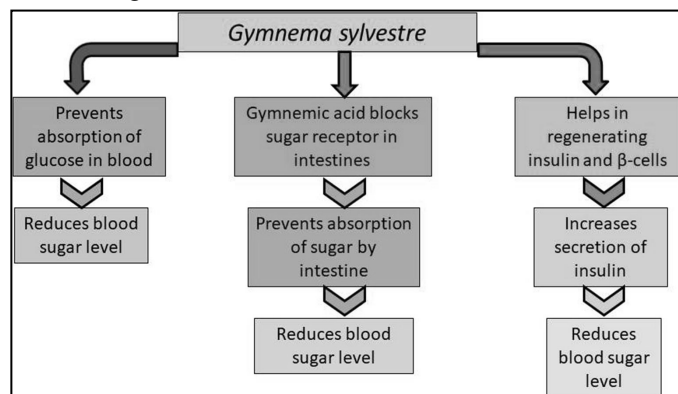


Figure 2 Mechanism of Action of *Gymnema Sylvestre* [15]

In this the main active constituents is Gymnemic acid which is mainly responsible for the anti-diabetic activity.

### 2.3. Mechanism of Gymnemic Acid

Gymnemic acid is a mixture of oleanan-class and dammaren-class triterpenoid saponins. Gymnemic acid and gymnemasaponin are subcomponents of oleanan saponin, and dammaren saponin is gymnemaside. Gymnemic acid I-VI was isolated from the aqueous leaf extract and gymnemic acid XV-XVIII was isolated and characterized from the leaf saponin fraction. Gymnemic acid VIII-XII has been elucidated as a glucosideuronic acid derivative of gymnemagenin. Gymnemic acid is thought to be involved in the antidiabetic activity of *G. Sylvestre*; gymnemic acid VIII was the main component of an extract that has been shown to activate the insulin release from the pancreas. *Gymnema* extract also contains Gymnemasaponin I-V, a group of anti-sweeteners with a new D-glucoside structure. Other plant compounds include flavone, anthraquinone, hentaicontane, pentatriacontane,  $\alpha$ - and  $\beta$ -chlorophyll, phytin, resin, decersitol, tartaric acid, formic acid, butyric acid, lupeol,  $\beta$ -amyryn-related glycosides and stigmasterol is included. [16]

The gymnemic acid is mainly found in shoot tips (54.29 mg-g-1 DW) and least in seeds (1.31 mg-g-1 DW). Antihyperglycemic effect of gymnemic acids includes a series of events starting from modulation of incretin activity which activates insulin secretion and release. So, it also enhances regeneration of pancreatic islet cells to increase enzyme mediated uptake of glucose. This process decreased glucose and fatty acid get absorbed in the small intestine and interferes in the capacity of receptors in mouth and intestine to sensation of sweetness. As per the previous report it is seen that the action of gymnemic acid is same to that of incretin-mimetic mechanism of action, in which

is it observed that gymnemic acid interact with glyceraldehyde-3-phosphate dehydrogenase (GAPDH), which is a main enzyme in glycolysis pathway. These observations also conclude that the acyl moieties present in gymnemic acids play important role for the GA-induced smearing of GAPDH and G3PDH and play an important role in the antidiabetic activity of GA derivatives [17]

It suppresses sweetness in humans. When leaf extract of plant, is taken by a diabetic patient, there is stimulation of the pancreas by virtue of which there is an increase in insulin release. These compounds have also been found to increase fecal excretion of cholesterol. This is reported that gymnemic acids have a ability to delay the glucose absorption in the blood. The atomic arrangement and the structure of gymnemic acid molecules is almost same as the glucose molecules. These molecules fill the receptors sites on the taste buds thereby halt the activation by sugar molecules present in the food, thereby curbing the sugar craving and it suppress the uptake of sugar molecules. Also, Gymnemic acid molecules occupies receptor location in the absorptive external layers of the intestine thereby preventing the sugar molecules absorption by the intestine, which results in low blood sugar level and hence helpful in the treatment of diabetes [18].

Several gymnemic acid homologues with different acyl groups were purified from the leaves of *G. sylvestre* and their structures were determined. Interestingly, deletion of the acyl group decreases the antidiabetic activity. It diminishes the sweetness of most of sweeteners, including the artificial sweeteners, for e.g.: aspartame and natural sweeteners, for e.g.: thaumatin, a sweet protein. [19]

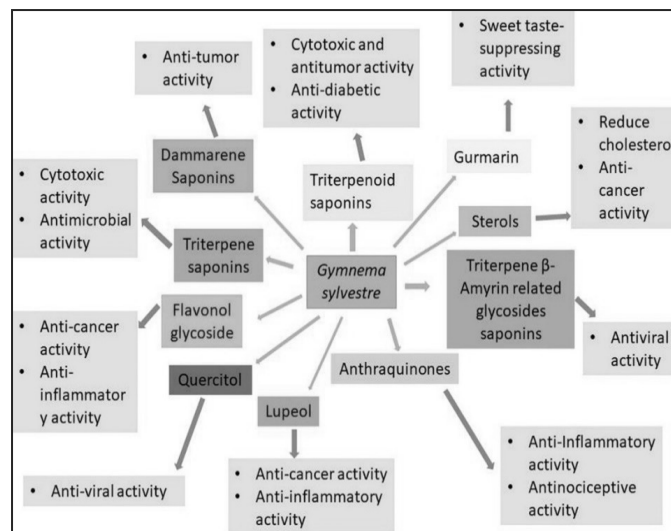


Figure 3 Uses of *Gymnema Sylvestre* [15]

In general, it is observed that the accumulation of the carbohydrates and fats is the main cause for obesity. Gymnemic acids works on interaction of carbohydrates to the receptors in the intestine, so “empty calories” are taken care due to which the body does not go into obese stage. The acids helps in curbing of diabetes by same mechanism as mentioned above for carbohydrate. Also now a days, the herb is traditionally used for the treatment of hyperglycemia in India and the extracts of

Gymnema as Gymnema Tea are used to control obesity which is a marketed product in Japan.

## 2.4. Uses

*Gymnema Sylvestre* can be employed as a sugar destroyer 'Madhumeha' in cases of glycosuria and other urinary disorders (because of chewing leaves. According to Sushruta and Ayurvedic Pharmacopeia of India, both the dried leaf and root part of gymnema medicinal plant is been useful in treatment of svasa (bronchial asthma), kasa (cough), kustha (leprosy and other skin diseases), and vrana (wounds), Dyspepsia, constipation, hepatitis, haemorrhoids, renal and vesicle calculi, cardiopathy, asthma, bronchitis, amenorrhea, conjunctivitis, and leukoderm are all other conditions which can be treated with this drug depends on dosage form and formulation type. Even many other properties like Bitterness, astringent, thermogenic activity, anti-inflammatory, digestive, liver tonic, diuretic, stomachic, stimulant, anthelmintic, laxative, cardio tonic, anti-pyretic, and uterine tonic, have been reported. (10,19,20). *Gymnema Sylvestre* have been presented in figure 3.

## 2.5. Adverse Effect

General: There is no clinically specific adverse effects related to oral gymnema in the available literature by the long-term use of *Gymnema Sylvestre*. Oral (taste effects): Gymnema has observed to possess a sweet-taste suppressing effect, due to peptide gurmarin. Endocrine: Ingestion of gymnema leaves occurs which have been found in the multiple animal testing.

## 3. SALACIA RETICULATA

*Salacia reticulata* also well known as Kothala himbatu belongs to family Hippocrateaceae has been used for several years against diabetes and other medical issues as well [22]. *Salacia* consisting various species are actively found in ayurvedic system for diabetes, gonorrhoea, rheumatism, itchin, asthma, ear diseases, leukaemia and various inflammations. [23]

### 3.1. Salacia Chinesis

It is known around as Saptarangi in Hindi and belongs to Hippocrateaceae, which has since been incorporated into the Celastraceae family. This medicinal plant has got numerous active constituents namely salacinol, kotalanol, neokotalanol, neosalacinol, Salaprinol, ponkoranol, foliasalaciosides, foliachinenosides and proanthocyanidin active against diabetes, hyperlipidemia, obesity, hepatotoxicity. [24]

### 3.2. Active Constituents:

The medicinal plants of *Salacia* species have got numerous active constituents, some of them namely Mangiferin (C<sub>19</sub>H<sub>18</sub>O<sub>11</sub>), Kotalanol (C<sub>12</sub>H<sub>24</sub>O<sub>12</sub>S<sub>2</sub><sup>+</sup>), Salacinol (C<sub>9</sub>H<sub>18</sub>O<sub>9</sub>S<sub>2</sub><sup>+</sup>). [15]. The extracts of *Salacia* species contain:

Neokotalanol, Ponkoranol, Neosalacinol, 26-hydroxy-1,3-friedelanedione, Salasol A. [25]

The methanolic extract of dried roots of *Salacia reticulata* yields multiple constituents, some of them namely are:

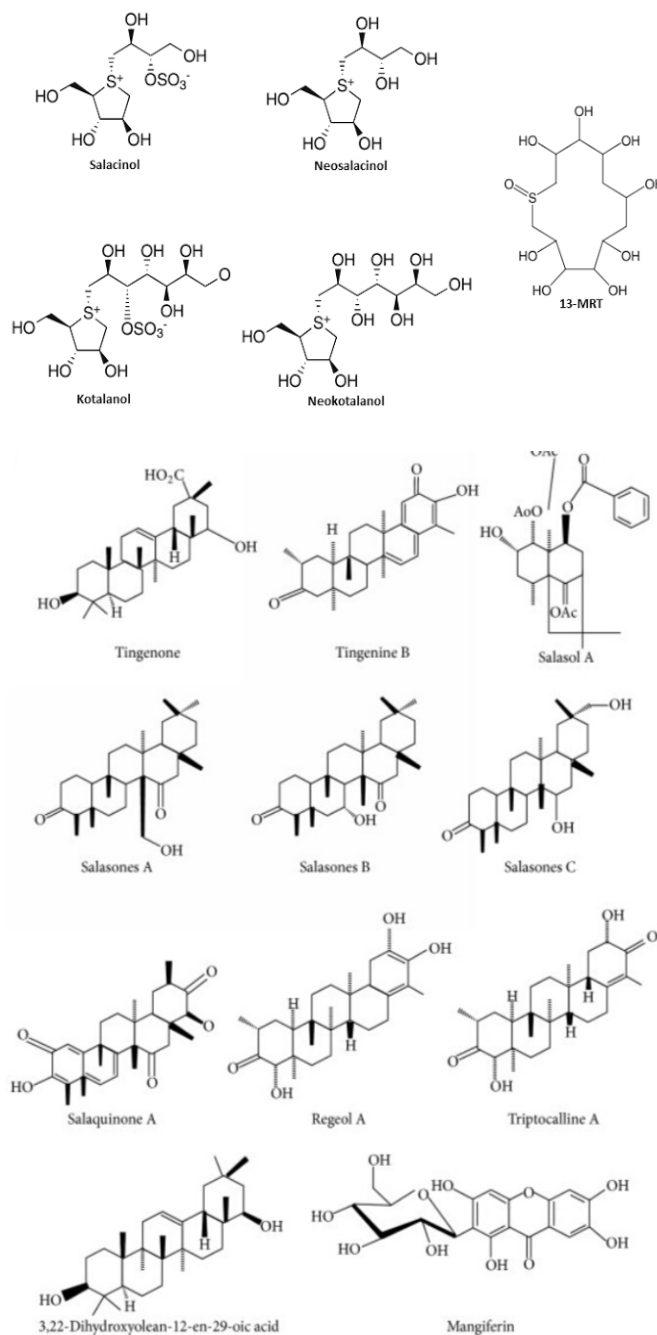


Figure 4 Active constituents of *Salacia* species [29]

Mangiferin, (-)-epicatechin, (-)-epigallocatechin, Lambertic acid, Salacinol, Maytenfolic acid, Kotalagenin 16-acetate. [26] The major Certain other active constituents found are-1,3 diktones, dulcitol, leucopelargonidine, glycosidal tannin, triterpenoids lambertic acid, etc. As per the chemical composition of species, root bark contains proantho-cyanidins that consists of monomeric leucopelargonidin, triterpenoids and glycosidal tannins. Further, the stem of the plant is known to be consisting gutta, dulcitol and proanthocyanidin. [23]

### 3.3 Mechanism of Action:

Salacia species are known for various therapeutic activities including anti-obesity, anti-inflammatory, anti-oxidant, hepatoprotective action along with major concern of our study, i.e., anti-diabetic activity.

- (a) The major hypoglycaemic effect of Salacia species is due to its alpha-glucosidase and amylase inhibition (salacinol, kotalanol). Inhibition of these intestinal enzymes delays glucose absorption and suppresses postprandial hyperglycaemia. [27]
- (b) Alpha-glucosidase inhibition prevents breakdown of oligosaccharides into monosaccharides and thus maintains normal human blood glucose level. Aldose reductase enzyme converts glucose into sorbitol which gets accumulated in lens causing cataract formation. This is prevented by aldose reductase inhibitory action of the constituent kotalgenin 16-acetate. [23]
- (c) Mangiferin gives anti-diabetic effect by activating PPAR-alpha-luciferase activity in human embryonic kidney 293 cells and enhances expression of PPAR-alpha-dependent lipoprotein lipase and its activity in THP-1 derived macrophage cell line.
- (d) Various countries including Japan and United States use this plant as a food supplement for the prevention of diabetes and obesity. [28]

### 3.4. Major Active Constituents:

The major constituents of Salacia species based on their variable therapeutic actions include, Mangiferin, Kotalanol, Salacinol.

Several targets for their observed activity are peroxisome proliferator-activated receptor-alpha-mediated lipogenic gene transcription, angiotensin II/ angiotensin II type 1 receptor, alpha-glucosidase, aldose reductase, pancreatic lipase, etc. [29]

- (a) **Mangiferin;** It is considered amongst the most potent active constituents due to its multi-target mechanisms. Anti-diabetic property is given by dose dependent down regulation of mRNA for this hepatic gluconeogenic enzyme-fructose-1,6-diphosphatase. This results in decrease in fasting blood glucose levels [24]. Another function as an immunoprotective is due to its free radical scavenging properties. It cause inhibition of induced oxidative stress in lymphocytes, neutrophils and macrophages lowering induced increase in lipid peroxidation and decrease in catalase and superoxide dismutase activities in these cells. Resultantly, protect oxidative damage to cardiac and renal tissues. [30] It also acts as anti-hyperlipidemic and anti-atherogenic agent by decreasing plasma total cholesterol, triglycerides, LDL cholesterol with elevations in HDL. [31]
- (b) **Kotalanol:** These active constituents are extracted from water soluble portion of Salacia species. Antidiabetic activity is due to their action against human intestinal maltase-glucoamylase. They effectively behave as al-

pha-glucosidase inhibitors Act against human intestinal maltase-glucoamylase. [32]

- (c) **Salacinol:** Another remarkable action given by kotalanol and salacinol is their inhibitory activity against pancreatic lipase and hence behave as anti-hyperlipidemic agents. [33] They are also known for their aldose reductase inhibitory action. [34] The above-mentioned active constituents are already known for their multi-target and effective actions in therapeutic field. Hence, they can be modified as per the future perspective for the betterment in regard of certain common diseases of the current scenario like diabetes, obesity, hyperlipidemia, cardiac diseases, etc.

### 3.5 Uses

Salacia species has numerous therapeutic uses.

- (a) Water extracts of Salacia reticulata leaves have ability to enhance plasma insulin level and lowers lipid peroxide level resulting in anti-diabetic and anti-obesity actions respectively.
- (b) This medicinal plant is known for its application in asthma, menstrual problems, joint pain, gonorrhoea and related issues.
- (c) It is widely used as a hepatoprotective agent.
- (d) Other uses include its action as anti-inflammatory, anti-proliferative, used against itching and swelling.

### 3.6. Side Effects

The safety of Salacia reticulata is known only for 6 weeks when taken orally. There is no further information for using it for a longer time period. [35] Common side effects associated with its use are gas, belching, abdomen pain, nausea and diarrhoea [36].

## 4. SWERTICA CHIRATA

Swertica Chirata originates from the family Gentianaceae, representing approximately 135 species. *Swertica Chirata* is known as Kirata Tikta in Ayurvedic texts. Swertica Churata is Carminative, laxative, antipyretic, Febrifuge, antiperiodic, anti-inflammatory and antihelmintic, used for the treatment and prophylaxis of ailments such as piles, skin diseases and diabetes. Whole plant of the Swertica Chirata is used for treatment. The species is critically endangered and found in the temperate regions of Himalayas over the altitude of 1200m to 3000m extending from the Kashmir Valley to Bhutan. Some species of Swertica bear purple and blue flowers and possess Medicinal and cultural uses. Swertica Chirata has reported to have wide number of pharmacological properties. The medicinal usage is documented well in many pharmacopeias, Indian Pharmaceutical codex, The British and The American Pharmacopeias. *S. Chirata* is an annual /binnenial herb which is approximately 0.6–1.5 m tall, the whole plant can be used for its medicinal properties [37-38]

#### 4.1. Medicinal Uses

*S. Chirata* is utilised in by numerous population group in numerous ways for various medicinal properties, the whole plant is widely used for its antiprophyllaxis and treatment of fever, malaria, anemia, liver disorders, skin diseases and bronchial asthma, hepatitis, epileps, hypertension, inflammatory and digestive diseases. [38] Ayush-64, Diabecon, mensturyl syrup a herbal formulation involve *S. Chirata* extract in different concentrations for its pharmacological use in different ailments. The contribution of this drug in the treatment of numerous ailments has been validated and recorded in ayurvedic system of medicines. The widespread usage of *S. Chirata* in traditional medicines has led to extensive chemical research of the plant, as well as the discovery of active components that give the plant its therapeutic characteristics. *S. Chirata* is also available as tinctures and infusions in British and American pharmacopoeias. Traditional treatments use the entire plant, but the root is said to be the most bioactive component.

#### 4.2. Pharmacological Uses

*S. Chirata* has been the subject of a number of pharmacological studies due to its many ethnobotanical uses. Previous study has shown that *S. Chirata* extracts have antibacterial, antifungal, antiviral, anticancer, anti-inflammatory, and other biological activities such as antidiabetic and antioxidant properties. [39-43] Simultaneously, a variety of in vitro and in vivo test systems have been used to assess *S. Chirata* pharmacological capabilities. Aqueous, alcoholic, and methanolic extracts of *S. Chirata* have a range of intriguing pharmacological effects, according to evidence-based laboratory experiments. The entire plant of *S. Chirata* has been reported to be utilised for antibacterial and antifungal treatment. [40,44-45]

#### 4.3. Phytochemical Constituents and their uses

The widespread usage of *S. Chirata* as a traditional medication, as well as its commercialization in modern medical systems, has prompted a surge in scientific research into its photochemistry in the hopes of identifying the active phytochemicals. As a result, a large body of literature has been written about the chemical contents of this plant. [46-51] The presence of a diverse group of pharmacologically bioactive components belonging to different classes such as xanthenes and their derivatives, lignans, alkaloids, flavonoids, terpenoids, iridoids, secoiridoids, and other such as chiratin, ophelicacid, palmitic acid, oleic acid, and stearic acid is attributed to *S. Chirata* wide range of biological Chiratanin, found in several areas of *S. chirayita*, was the first dimeric xanthone to be isolated. [53] The biological activity of important phytoconstituents such as amarogentin, swertiamarin, mangiferin, swerchirin, sweroside, amaroswerin, and gentiopiricin has been partly linked to the pharmacological efficacy of *S. chirayita*. Amarogentin has been studied for its anti-hepatitis, anticancer, and antileishmanial properties [52], whereas swertiamarin has been investigated for its anti-hepatitis, anticancer, and anti-arthritic properties. It has been demonstrated to have anti-diabetic effects. Mangiferin

has anti-diabetic, anti-atherosclerotic, anti-cancer, anti-HIV, anti-parkinson, and chemo preventive properties. Swerchirin has antimalarial, hypoglycemic, hepatoprotective, and pro-hematopoietic properties, as well as blood glucose lowering and chemopreventive pharmacological effects. Swerchirin (at various doses) increased glucose-stimulated insulin release from isolated islets substantially. Sweroside has been suggested as a possible osteoporosis therapeutic natural medication because it is antibacterial and preventative in the treatment of hyperpigmentation. The bitter components in amaroswerin are renowned for their gastroprotective properties.

#### Following are the chemical constituents present in *S. Chirata*

Amarogentin, Swertiamarin, Magneferin, Swerchirin, Sweroside, Amaroswerin, Oleanolic acid, Ursolic acid, Swertanone, Syringaresinol., Bellidifolin, Isobellidifolin, 1-Hydroxy-3,5,8-trimethoxyxanthone, 1-Hydroxy-3,7,8-trimethoxyxanthone, 1,5,8-trihydroxy-3-methoxyxanthone, B-Amyrin, Chiratul.

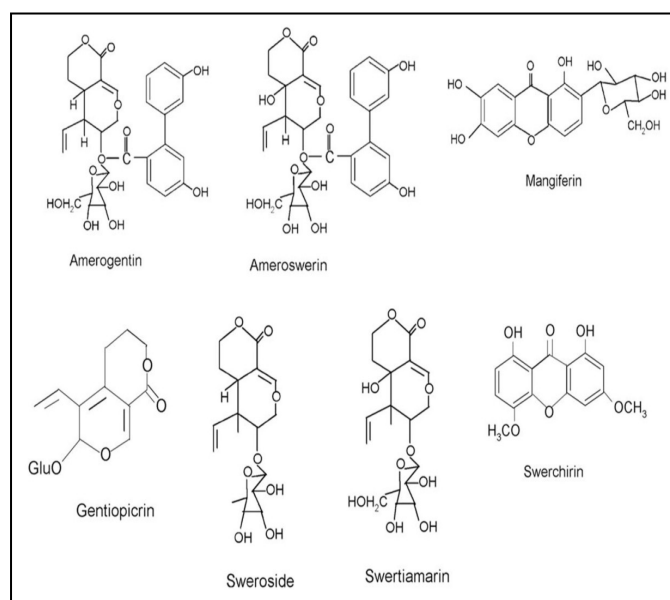


Figure 5 Active constituents of *Swertica Chirata*

#### 4.4. Mechanism of Active Constituents

- Swertiamarin:** Adipogenesis is induced by gentianine, a metabolite of swertiamarin, via upregulating the gene expression of PPAR-g, GLUT-4, and adiponectin. In completely differentiated adipocytes, gentianine treatment boosted PPAR-g expression. Up-regulation of PPAR-g expression has been found to improve insulin sensitivity. [53]
- Amarogentin:** Amarogentin inhibits the enzyme aldose reductase and thus acts as an antidiabetic, but the exact mechanism of action is still unknown. Aldose reductase (ALR2) is a key enzyme in the polyol pathway, activation of aldose reductase under hyperglycemic conditions contributes to the development of chronic diabetic complications. [54]

## 5. PTEROCARPUS MARSUPIUM

*Pterocarpus marsupium* Roxb (Sanskrit: Pitasala) (Leguminosae), also known as Indian kino or Bijasar, is a large tree common to the mixed deciduous forests of central and Peninsular India [55]. *Pterocarpus marsupium* Roxb. is traditionally used in Indian folklore medicine for the treatment of diabetes [56]. It is well known to Ayurvedic medicine because of its curative and lenitive properties. Its flowers are employed against fever, its heartwood as depurative, hemostatic, and rejuvenating, its wood is used for chest and body pain as well as indigestion, etc. The bark of *P. marsupium* is very effective in preventing cataract formation and reducing hyperglycemia in alloxanized diabetic rats [57] and the heartwood is useful as hypoglycemic agents [58].

### 5.1. Active Constituents

*Pterocarpus* is a rich source of polyphenolic compounds. All active principles of *Pterocarpus marsupium* are thermostable. The plant contains pterostilbene 4-5%, alkaloids 0.4%, tannins 5%, protein, pentosan, pterosupin, pseudobaptigenin, liquiritigenin, isoliquiritigenin, garbanzol, 5-de-oxykaempferol, Phydroxybenzaldehyde, beudesmol, erythrodiol-3- monoacetate, l-epicatechin, marsupol, carpusin, propterol, propterol B, marsupinol, irisolidone-7- O-A-L-rhamnopyranoside, have been obtained mainly from the heartwood and root. The gum kino from the bark provides nonglucosidal tannins. The main constituents are:

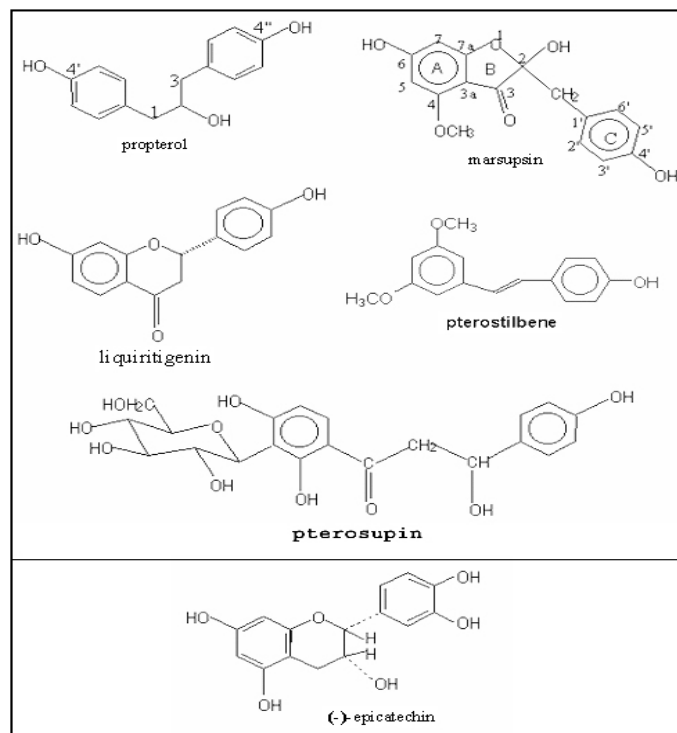


Figure 6 Chemical constituents of *Pterocarpus marsupium*

### 5.2. Mechanism of Action

*P. marsupium* demonstrates unique pharmacological properties, which include beta cell protective and regenerative properties as

well as blood glucose lowering activity. *P. marsupium* was found to reverse the damage to the beta cells and actually repopulate the islets, causing a nearly complete restoration of normal insulin secretion. [56-60]

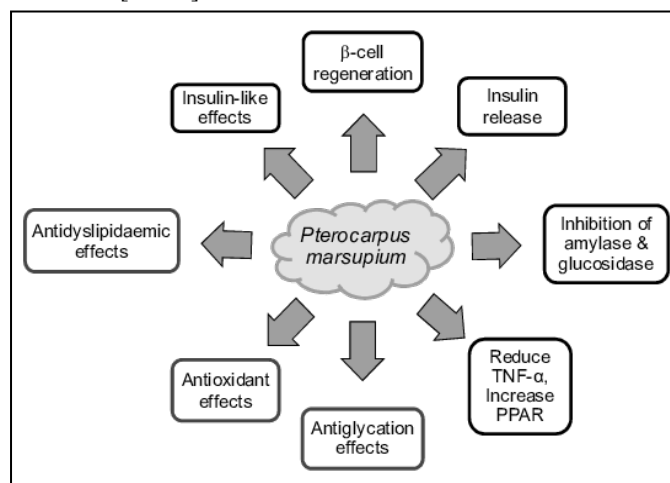


Figure 7 Antidiabetic effects of *Pterocarpus marsupium*

### 5.3. Medicinal Uses

Various parts of the *P. marsupium* tree have been used as traditional ayurvedic medicine (Table 1). The bark is used for the treatment of stomach-ache, cholera, dysentery, urinary complaints, tongue diseases and toothache. The gum exude 'kino', derived from this tree, is used as an astringent. [61-64]. The gum is bitter with a bad taste. However, it is antipyretic, anthelmintic and tonic to liver, useful in all diseases of body and stypitic vulnerate and good for griping and biliousness, ophthalmia, boils and urinary discharges. The flowers are bitter, improve the appetite and cause flatulence. [65].

Table 1: Medicinal uses of *P. marsupium*

Part	Medicinal use
Leaf	External application for boils, sores and skin diseases, stomach pain
Bark	Astringent, toothache
Flower	Fever
Gum-Kino	Diarrhea, dysentery, leucorrhoea, passive haemorrhages

### 5.4. Adverse Effect:

The absence of abnormal blood cell counts and blood chemistry values and the absence of extract-related adverse effects [66]

## 6. CONCLUSION

Diabetes Mellitus is a severe endocrine disorder that affects about 10% of the global population and has recently become a major source of worry. Diabetes mellitus is a metabolic condition that affects the body's ability to produce and use insulin. Gymnemic acid, *Salacia Reticulata*, *Salacia chinensis*, *Swertica Chirata*, and *Pterocarpus marsupium* have all been mentioned in this article.

“*Gymnema Sylvestre*” is one of the most promising medicinal plants. Gymnemic acids’ antihyperglycemic impact is the result of a cascade of processes that begin with the modification of incretin activity, which promotes insulin secretion and release. As a result, it boosts the regeneration of pancreatic islet cells, which increases glucose uptake through enzymes. This mechanism reduces the amount of glucose and fatty acids absorbed in the small intestine. “*Salacia Reticulata*” *Salacia* species medicinal plants include a variety of active components, including Mangiferin (C<sub>19</sub>H<sub>18</sub>O<sub>11</sub>), Kotalanol (C<sub>12</sub>H<sub>24</sub>O<sub>12</sub>S<sup>2+</sup>), and Salacinol (C<sub>9</sub>H<sub>18</sub>O<sub>9</sub>S<sup>2+</sup>) Alpha-glucosidase and amylase inhibition are the main hypoglycaemic effects of *Salacia* species (salacinol, kotalanol), Inhibition of these intestinal enzymes reduces postprandial hyperglycemia by delaying glucose absorption. Inhibition of alpha-glucosidase prevents the breakdown of oligosaccharides into monosaccharides, Mangiferin inhibits diabetes by increasing the activity of the PPAR-alpha-luciferase gene in the human embryonic kidney. Another herbal drug “*Swertica Chirata*” originates from the family Gentianaceae, representing approximately 135 species. *Swertica Chirata* is known as Kirata. Tikta in Ayurvedic texts. “Swertiamarin:” Gentianine, a metabolite of swertiamarin, causes adipogenesis by upregulating the gene expression of PPAR-g, GLUT-4, and adiponectin. It has been discovered that increasing PPAR-g expression improves insulin sensitivity. Amarogentin works as an antidiabetic by inhibiting the enzyme aldose reductase, however the specific mechanism of action is uncertain. The polyol pathway enzyme aldose reductase (ALR2) is activated in hyperglycemic circumstances, which leads to the development of chronic diabetes problems. “*Pterocarpus marsupium*”, often known as Indian kino or Bijasar, is a huge tree native to Central and Peninsular India’s mixed deciduous woods. *P. marsupium* has pharmacological capabilities that are unique, including beta cell protection and regeneration, as well as blood glucose reducing activities. *P. marsupium* was discovered to reverse beta cell damage and repopulate islets, resulting in a near-complete restoration of normal insulin output. The advancement in the metabolic damage that diabetes causes can’t be undone but reduced by the use of these drugs which potentially show their effectiveness with proof.

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Review Article

## HERBAL APPROACH FOR THE MANAGEMENT OF PSORIASIS

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### ABSTRACT

Psoriasis is a common persistent, non-communicable skin illness that is influenced by genetic, immunological, and environmental factors. Pathophysiology of the disease includes mainly activated T cells into the dermis and release of cytokines from keratinocytes that lead to rapid growth of skin cells. Psoriasis is an inflammatory skin condition that causes viable factors including skin trauma, infection, emotional stress, alcohol abuse, medicines. There are various kinds of psoriasis such as plaque psoriasis, guttate psoriasis, scalp psoriasis, nail psoriasis, psoriatic arthritis, flexural psoriasis. Psoriasis can be treated with a variety of methods, including light therapy, topical medications, systemic medicines, and a homoeopathic approach. The therapeutic agents that either modulate the immune system or normalize the differentiation of psoriatic keratinocytes.

## 1. INTRODUCTION

Psoriasis is a chronic, non-infectious skin disease characterised by patches of thick red skin covered in silvery white plaques caused by T cell-mediated keratinocyte hyperproliferation [1]. The name “psoriasis” comes from the Greek word “psora,” which meaning “itch” [2]. Psoriasis is a widespread long-term skin disorder that has no cure, and the treatments available only relieve the symptoms. Psoriasis can be treated with a variety of methods, including light therapy, topical medications, systemic treatments, herbal medicines, and a homoeopathic approach. It is characterized by having non-communicable skin disease in which red scaly patches appear on any part of the body, face, lower back and soles of the feet and less common mouth and the area around genitals [3, 4]. The nails are the most commonly affected places, followed by the scalp, elbows, and knees. Excessive growth of epidermal cells leads in scales and red patches in this illness, which is referred to as plaque psoriasis [5]. Plaques usually appear on the skin of the scalp, elbows, knees and lower back. Psoriasis can also cause inflammation of the joints, which is called as Arthropathic psoriasis. Psoriasis is an autoimmune disease in which both genetic, immunological and environmental influences have a critical role. Psoriasis is an inflammatory skin condition that causes skin trauma, infection, emotional stress, alcohol abuse and medicines. psoriasis is one of the most very old disease continues now with the research of a good remedy [5].

### 1.1 Epidemiology of psoriasis:

Psoriasis is a skin disorder that affects about 125 million people of worldwide i.e 2 to 3% of the total population [6]. Although the disease is known to have higher prevalence in the polar regions of the world. The prevalence of psoriasis may vary from region to region due to variable environmental and genetic factors [7]. It has higher chances in females than males. Psoriasis does not spread from one person to another but it can be transmitted genetically [8].

- Psoriasis affects both sexes equally
- Around one-third of people with psoriasis report a family history of the disease.
- It can occur at any age [most commonly appears for the first time between the ages of 15 to 25 year.
- Onset with a second peak occurring at 55-60 years.
- It occurs mostly in the third decade of life [9]

### 1.2 Types of Psoriasis

- (a) **Psoriasis Vulgaris** : It is also known as plaque psoriasis is the most common type of psoriasis. It affects approximately 85% of the people. It can cover large area of skin. Most common sites include scaly plaques on the trunk and extensor surfaces of the limbs [10]. It is appear as red or

salmon pink in color covered by silvery patches and may be thick, thin large or small. Location :elbows, scalp, lower back and soles of the feet [11].

- (b) **Guttate psoriasis :** Guttate psoriasis is a type of psoriasis that appears as tear drop-shaped bumps on the skin that have fallen down on the body .Guttate psoriasis affects approximately 10% of the people and it is second most common type of psoriasis which is usually seen in children and young adult [12]. It is not common as plaque psoriasis.

There are three stages of guttate psoriasis:

1. Mild-cover about 3% of skin
2. Moderate-cover about 3-10% of skin
3. Severe-more than 10% and may be cover your entire body.

Guttate psoriasis is often triggered by bacterial streptococcal infections[strep throat] or viral respiratoryinfection [12].

- (c) **Inverse Psoriasis :** It is also known as flexural psoriasis. It appears as a smooth, shiny skin usually found in skin folds of the body such as armpits, under the breast and groin [13]. In inverse psoriasis complications include itching, fungal infections, and irritation.
- (d) **Pustular psoriasis:** It appears as a smooth, shiny skin usually found in skin folds of the form of psoriasis and present with widespread blisters of pustules [white pustules surrounded by red skin]. the skin becomes dry, red and tender. Generalised pustular psoriasis may affect randomly on any part of the body and comes with a fever, chills, severe itching, rapid pulse rate and muscle weakness. It can develop life threatening complications such as electrolyte balance and bacterial infection. Pustular psoriasis can be triggered by pregnancy emotional stress and infection Pustular psoriasis can be localized commonly to palms of the hand and soles of the feet which is known as palmoplantar pustulosis [14].
- (e) **Erythrodermic psoriasis:** Generalized Erythrodermic psoriasis is the most rare types psoriasis that looks like severe itching, burns, swelling and pains. It may affects large portions of the body and it spreads quickly. It can disrupt the body's ability to regulate temperature and for the skin to perform barrier function. Erythrodermic psoriasis is one of the most severe form of psoriasis that can lead to severe infections, including pneumonia and sepsis and congestive heart failure [15].
- (f) **Nail Psoriasis :** Nail psoriasis can affect the finger and toenails. The most often signs of nail psoriasis are pitting ,onycholysis, discolored nails and changes in nail shape and thick [16].

### 1.3 Pathophysiology of psoriasis

Psoriasis is recognized as the most prevalent auto immune disease caused by inappropriate activation of the cellular immune system. Psoriasis include mainly activated T cells in the dermis

and release of cytokines from keratinocytes that lead to rapid growth of skin cells. Normally the skin cells mature and are shed from the skin's surface every 28 to 30 days. When psoriasis develop the skin cells pile up, causing the visible lesion [17]. The pathophysiology of psoriasis must be understood in terms of the prominent pathologies occurring in both major components of the skin of epidermis and the dermis. There are two main hypotheses about the process that occurs in the development of the psoriasis. The first hypothesis is that psoriasis is primarily a disorder of excessive growth and reproduction of skin cells and The second hypotheses see the disease as being an immune-mediated disorder in which the excessive reproduction of skin cells is secondary to produce by the immune system [18].

#### Causes :

The exact cause of psoriasis is not clearly understood, but it is believed to have a genetic component and auto immune reaction. Psoriasis contains high level of compounds called leukotrienes. It is inflammatory mediators formed in leukocytes by the oxidation of arachidonic acid in the body. It is found in animal fat which include an autoimmune disease, emotional stress, hormones, skin injury, smoking, alcohol abuse, medicines including lithium and antimalarial drugs have been reported to trigger the diseases. Psoriasis is an immune system problem which causes skin cells to regenerate faster than normal rates [19].

### 1.4 Sign and symptoms

Psoriasis sign and symptoms can vary from person to person.

*Common sign and symptoms include:*

- Red patches of skin covered with thick, silvery scales.
- Small scaling spots [commonly seen in children]
- Dry, cracked skin that may bleed or itch
- Itching, burning or soreness
- Thickened, pitted or ridged nails
- Swollen and stiff joints

### 1.5 Treatment :

Psoriasis is a skin disorder that often comes and goes and there is no cure for psoriasis, but the available therapies, only relieve the symptoms. Treatment aims to stop the growth of skin cells and to reduce scales.

Psoriasis treatment is divided into three main types:

- Topical treatment
- Light therapy
- Systemic medications

#### (i) Topical treatment:

- **Corticosteroids:** They are the most frequently prescribed medications for treating mild to moderate psoriasis. They are available as ointments, creams, lotion, foam, sprays, and shampoos.

- **Coal tar:** Coal tar is the dry distillation product of organic matter heated in the absence of oxygen. Coal tar, in concentrations 5-20% can be compounded in creams, ointments, shampoos and in paste.
- **Tazarotene:** Tazarotene is a synthetic retinoid. It reduces mainly scaling and plaque thickness, with limited effectiveness on erythema. Tazarotene is available as a gel and cream and applied once or twice daily [20].

#### (ii) Light therapy:

Light therapy is the first line therapy for moderate to severe psoriasis, either alone or combination with medications.

- **Sunlight:** Ultraviolet light is a wavelength of light in a range too short for human eye to see. When exposed to the UV light, the activated t-cells in the skin are destroyed which leads to reduced scaling and inflammation.
- **Ultraviolet board band phototherapy:** UVB phototherapy is also called "Broadband UVB" can be used to treat single patches and psoriasis resistant to topical treatment.
- **Ultraviolet-A:** UVA light penetrates deeper in skin and makes more responsive to UVA exposure [21].

#### (iii) Systemic medication:

Psoriasis which is resistant to topical treatment and phototherapy is treated by medications that are taken internally by pill or injection. This is called systemic treatment.

- **Methotrexate:** This anti-metabolite is a very effective agent for treating psoriasis. It helps psoriasis by reducing the production of skin cells and suppressing inflammation.
- **Cyclosporine:** Cyclosporine suppresses the immune system and is similar to methotrexate in effectiveness. Major toxicities associated with cyclosporine therapy include nephrotoxicity and hypertension.
- **Oral retinoids:** Retinoids are known to have immunosuppressive and anti-inflammatory activity and to modulate epidermal proliferation and differentiation [22].

#### (iv) Herbal Medicines

The Herbal medicine is one of the oldest forms of medical treatment in human history. Medicinal herbs can be a good alternative for many diseases and conditions. They are low in cost and tend to have fewer side effects as compared to synthetic drugs. Natural medicines having a great source of easily available and effective therapy for skin disorders and it has been used for thousands of years. There are various herbal treatments of psoriasis which are useful for reducing the growth of skin cells and to reduce scales.

- (a) **Aloe vera-** Aloe vera is a very safe and natural remedy for psoriasis. It is a medicinal plant and has been used since ancient times to treat various health conditions. It has wound healing and anti-inflammatory properties thus it is an effective and safe remedy for psoriasis.

- (b) **Oregano oil-** Oregano oil is an herbal supplement. It is an effective antifungal agent and has natural antibacterial properties which are useful in the treatment of psoriasis.
- (c) **Chamomile-** It is an anti-inflammatory herb applied as a cream.
- (d) **Lavender-** It is an anti-inflammatory oil mixed with olive oil and applied to the affected areas.
- (e) **Curcuma longa/curcuma domestica-** Turmeric has a unique antibacterial and anti-inflammatory properties, turmeric helps to relieve the swelling pain and inflammation associated with arthritis.

#### (v) Herbs for External used in Psoriasis:

- (a) **Aloe vera:** It is an effective remedy for treating psoriasis. Applied in gel form to reduce inflammation and also improve hydration.
- (b) **Chamomile:** It is an anti-inflammatory and antibacterial herb applied as a cream.
- (c) **Lavender:** It is an antiseptic and anti-inflammatory oil mixed with coconut oil and massaging the mixture to the affected areas of the skin.
- (d) **Almond oil:** Applied after using other herbs for soothing dryness that comes along with psoriasis.
- (e) **Oatmeal:** It helps to reduce skin swelling and itching.

#### (vi) Herbs to take Internally for Psoriasis:

- (a) **Milk thistle:** It is one of the most powerful herbs. It can help regenerate and repair damaged liver cells. Taken as a tea and capsule.
- (b) **Berberine** (Oregon grape, barberry, gold thread): Anti-inflammatory, antioxidant and prevents toxin formation in the bowel. Use as a tea or tinctures or capsules.
- (c) **Purslane:** It contains high quantities of vitamins A, C & E which support skin health.

## 2. CONCLUSION

From different studies, it is evident that the activity of psoriasis is important. Medicinal plants, herbs are known to Ayurveda in India since ancient times. All the Ayurvedic therapies adopted as a part of various research studies proved to have significant results in the management of psoriasis. Psoriasis is a dreadful disease affecting physical, mental and social status of victims. A review of alternative natural therapies provides some options for increasing safety and efficacy in the management of psoriasis. This review will surely prove to be an eye-opener for patients suffering from psoriasis as well as the medical practitioners, pharmacists, nurses and other persons involved in the treatment of psoriasis and help them to understand the disease in a much better way to carry out safe and effective treatment of the disease.

## 3. ACKNOWLEDGEMENT

None.

#### 4. CONFLICT OF INTEREST

The authors declare no conflict of interest.

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