A Study of Certain Ayurvedic Plants Containing Steroidal Saponins with Anti Inflammatory Activity

Review Article

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Abstract

Inflammation is the local reaction of living tissue. The bacterial infections without inflammation would remain un encountered, such kinds of wounds will never heal, the tissues get injured and the organs might be permanently damaged. Detailed investigations have been undertaken on several plants for Anti - inflammatory activity. The most common screening model has been the prevention of Carrageenan induced edema in rats. The pure compounds investigated for Anti - inflammatory activity had diverse chemical structures. Extensive research has been carried out in the membrane permeability, immune stimulant, Hypo cholesterolemic, Anti-inflammatory properties of Saponins. In the plant kingdom large number of biologically active compounds like Saponins glycosides are present. Most of the plants having Saponin glycosides are medicinally important. Many glycosides are used in traditional and modern medicines because of their cardio tonic, analgesic, anti-rheumatic other useful actions. The present study is therefore focussed on discussing the various Ayurvedic medicinal plants having Saponins with Anti-inflammatory action. Method: Classical Ayurvedic texts along with the commentaries and modern literature was collected from Modern books, Journals were carefully studied to compile information about plants containing Saponins and to evaluate with Anti-inflammatory action. It was observed that these Saponin containing plants having different karmas and these karmas having Sotha hara property (Anti-inflammatory activity). Results and conclusion: The below mentioned 10 plants are time tested and mentioned in the classical literature and indicated in many inflammatory disorders with significant rate of success. The study helps to establish a potent drug from the existing formulary.

Keywords: Medicinal plants, Chemical constituents, inflammation, Saponins, Research activity of plants.

Introduction

Inflammation is the most common and most important of all disease processes. Inflammation is our safeguard against injury (1). Inflammation is best defined as the reaction of vascularized living tissue to local injury (2). Inflammation is the local reaction of living tissue to injury (3). The inflammatory reaction is, at first, local, consisting primarily changes in the blood vessels, the escape of cells and fluid from the blood into the tissues and the consequent changes in the tissues. The reaction of living tissue to injury which comprises a series of changes of the terminal vascular bed, blood and connective tissues, which tend to eliminate the injurious agents to repair the damaged tissue, may be called as inflammation (4).

Causes:

The causes of inflammation are multitudinous.
Most frequent causes of inflammation are trauma.

The minor injuries that escape our attention as well as those that attract our notice and infection by bacteria, viruses, fungi or parasites.

Exogenous and endogenous, such as irradiation, poisoning, metabolic disorders and derangements of the immune system (5).

Types:

Acute inflammation - Short duration.
Chronic inflammation - longer duration.

Acute inflammation reactions are redness, pain, swelling and loss of function. The intensity and the localization of the reaction are determined by both severity of the injurious agent and the reactive capacity of the host. Chronic inflammation is also characterized by pain, redness and swelling but it does not subside in a period of days. Humans owe to inflammation and repair their ability to contain injuries and heal defects. Without inflammation, infections would go unchecked, wounds would never heal and injured organs might remain permanent festering sores. The inflammatory reactions underlie the genesis of rheumatoid arthritis, life – threatening hypersensitivity reactions and some forms of fatal renal disease. Reparative efforts may lead to disfiguring scars or fibrous bands that cause intestinal obstruction or limit the mobility of joints (6). Varieties of inflammation: A number of terms are used to describe the varieties of inflammation seen clinically.

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One speaks of serous inflammation if the inflammatory exudate is thin and watery, as is often the case with streptococcal infections. If pus is formed, the inflammation is called purulent or suppurative. If there is necrosis of the superficial part of an epithelium with intermixture of fibrin to give a membrane overlaying the lesion, as in diphtheria or ischemic enteropathy, the inflammation is called membranous, pseudomembranous or diphtheritic, and the membrane is sometimes called a false membrane. An inflammation that spreads diffusely through the connective tissues is called cellulitis (7).

Mediators of inflammation:

Mediators of inflammation released from cells are histamine, serotonin, prostaglandin and lysozomal enzymes. Mediators derived from plasma are four major ‘cascade’ systems – the clotting, fibronolytic and kinin and complement systems. The agents that cause the changes in inflammation- the alteration in the blood vessels, the escape of proteins and cells into the tissues, the changes in the tissues- are called the mediators of inflammation (8).

They are many active phytochemical constituents of individual plants are insufficient to achieve the desirable therapeutic effects. In this phytochemical constituents saponins are occur widely in plant species. The many plants used worldwide in traditional medicine contain triterpene saponins, which can often account for their therapeutic action, including anti-inflammatory properties.

Saponins:

Saponins are plant glycosides that derive their name from their soap like properties. As the name indicates, the aglycone part of these glycosides has soap like action (9). Such plants contain a high percentage of glycosides known as saponins (Latin sapo, soap) which are characterized by their property of producing a frothing aqueous solution (10). They exhibit some physical properties like foaming action by shaking with water and yielding colloidal solutions. They are generally considered as Hemotoxic because they cause haemolysis of erythrocytes. Saponins have a bitter and acrid taste. They are mostly non crystalline substances soluble in water and alcohol, but insoluble in non-polar organic solvents. Chemically, they contain aglycone called as sapogenin. Sapogenins are high molecular weight substances which by acetylation give crystalline forms (11).

Role of Saponins in plant:

The Saponins have multiple effects on animal cells and on fungi and bacteria and only a few have addressed their function in plant cells. Many saponins are known antimicrobials they also inhibit fungus, and protect plants from insect attack.

Saponins may be considered a part of plants and as such have been included in a large group of protective molecules found in plants named ‘Phyto protectants’. The first term describes those Saponins, such as A and B avenacosides in oat, that are activated by the plants enzymes in response to tissue damage or pathogen attack (12).

Image No.1 Classification of saponins (13)

Depending on the nature of aglycone (Image no 1), saponins are categorized into 2 groups viz

- Pentacyclic triterpenoid saponins
- Steroidal saponins (tetracyclic triterpenoid saponins)

Both types of aglycone are linked with different types of sugars and uronic acids.

Pentacyclic triterpenoid Saponins:

This group contains the Sapogenin with Pentacyclic triterpenoid nucleus, which is linked with sugars or uronic acids. The sapogenin is further differentiated into

- α – amyrin type
- β –amyrin type
- Lupeol (14).

An important derivative of this group is triterpenoid acids. These acids are present in various drugs formed by substitution of carboxylic group at C4, C17 and C20.

Besides the chemical structure, these types of saponins differ from steroidal saponins by way of their distribution. Pentacyclic triterpenoid saponins are available from various families of dicot plants like Polygalaceae, Berberidaceae, Umbelliferae, Rubiaceae, Compositae, Rutaceae etc., (15).

Steroidal saponins:

Commercially, steroidal saponins are of great pharmaceutical importance, as they are used as raw material for the synthesis of various medicinally useful steroids like vitamin D, cardiac glycosides, corticoids like betamethasone and cortisone acetate, sex hormones like progesterone, testosterone and oestradiol, oral contraceptives such as mestranol and norethisterone (16); and Spiro lactone which is a diuretic steroid. Steroidal Sapogenins viz. diosgenin and hecogenin can be considered as a representative example of this group of saponins. Due to their pharmaceutical importance, many plants have been screened for detection of steroidal saponins. While steroidal saponins are common in plants used as herbs or for their health promoting properties. Their distribution is limited to plant kingdom. In dicot plants important sources are from Leguminosae, Solanaceae and Apocynaceae (17).
Biogenesis of Steroidal saponins:
Steroidal saponins arise via the mevalonic acid pathway. A scheme for the subsequent cyclization of Squalene to give cholesterol is illustrated. Cholesterol, the wide distribution of which in plants has only relatively recently been shown, can be incorporated into a number of C27 Sapogenins without side-chain cleavage, although it is not necessarily an obligatory precursor (18).

Natural steroids for the production of pharmaceuticals:
The range of steroids required medicinally, cortisone and its derivatives are 11-oxosteroids, whereas the sex hormones, including the oral contraceptives and the diuretic steroids have no oxygen substitution in the C-ring (19).

Biological effects:
1. Anti-inflammatory.
2. Hypolipidemic activity.
3. Antifungal activity.
4. Anti-microbial activity.
5. Virucidal activity.
6. Effect on cholesterol Metabolism.
7. Hypoglycaemic activity.

Anti-inflammatory activity:
The significant ameliorative activity of the Saponins may be due to inhibition of the mediators of inflammation such as Histamine, Serotonin and Prostaglandin along with its antioxidant property which inhibits the formation of ROS (Reactive Oxygen Species) which also play a major role in inflammation (20). A high Saponin diet can be used in the in the inhibition of dental caries and platelet aggregation, in the treatment of Hypercalciuria in humans and as an antidote against acute lead poisoning. In epidemiological studies, saponins have shown to have an inverse relationship with the incidence of renal stones (21). Other biological activities of saponins are also responsible for lowering cancer risks by lowering blood cholesterol levels. Saponins are responsible for many other important activities molluscidal, anthelmintic, anti ulcerogenic, anti-cancer, antioxidant, immunomodulatory, anti-bacterial, anti-malarial, analgesic, Hepatoprotective (22).

The below mentioned plants possess the karmas like Sothahara, Vranahara, Visarpahara, Slipadahara, Mutrakrcchra, Amavatahara. All the karma can be considered under Sothahara karma.

Sotha:
The aggravated Vayu brings the vitiated rakta, pitta and kapha to the outer veins which block the former resulting in the Swelling due to deposition in the above in the skin and muscle tissue (23).

Slipada:
Excessively painful Swelling in the groin, spreading gradually to leg and associated with fever is called Slipada (24). Vranahara: The inflammation that occurs in a particular area is considered as a premonitory symptom of an wound (25).

Mutrakrcchra:
Means difficulty in urination. There is heaviness and Swelling in the bladder and penis and the urine is frothy in kapha type of mutrakrcchra (26).

Visarpahara:
Rakta, lasika, twak and mamsa are the dhusya (vitiating factors) and the tridosas are the turbid factor. All these seven important factors take part in the origination of the disease Visarpa. And other symptoms swelling, pulsation, pinning sensation, breaking sensation, fatigue and pain (27).

Amavata:
Vata and ama get aggravated simultaneously and get seated in the trika sandhi (sacrum). Then these two (vata and ama) make the body rigid. This disease is called Amavata. It causes painful Swelling (inflammation) in the joints of hands, legs, ankle, sacrum, knees where the morbid substance gets seated (28).

Most of the plants containing Saponin glycoside are medicinally and commercially important. Commercially steroidal saponins are more important as they are used as raw material for the synthesis of various medicinally useful steroids like Vit D; cardiac glycosides corticoids like betamethasone and cortisone acetate etc. and due to their pharmaceutical importance, many plants were screened to detect steroidal saponins. Solanum species: This large genus is noted for the production of C27 steroidal alkaloids in many species. Some of these alkaloids are the nitrogen analogues of the C27 Sapogenins (e.g: solasodine and diosgenin) (29). Anti-inflammatory activity of Saponin may be due to inhibition of the mediators of inflammation such as histamine, serotonin and prostaglandin along with its anti-oxidant property which inhibits the formation of ROS (Reactive oxygen species) which also play a major role in inflammation.

Aims and Objectives
To find out good anti-inflammatory activity of the drugs with contains steroidal saponins to the literary survey.
To collect the information regarding the selected drugs from the Research point of view.

Materials and Methods
The present study Aimed to collect relevant literature from various sources, including Ancient textbooks along with recent evidences in the context.
Ayurvedic literature was collected from either Samhitaw or Commentaries. Modern literature was collected from modern books, Journals. All information was collected, Analysed and interpreted.
The below mentioned following medicinal plants contain Steroidal Saponin with anti-inflammatory Action.

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### Results

Table No. 1. Showing Saponin containing plants with Anti-inflammatory action.

| S.No | Sanskrit name | Scientific name / Family | Part used / Chemical constituents | Indications | Therapeutic uses | Research activity |
|------|---------------|--------------------------|-----------------------------------|-------------|-----------------|-------------------|
| 1.   | Kebuka        | *Costus speciosus* (Koen. ex Retz.) Sm.\ Costaceae | Seeds: Dioscin, prosapogenins-A and B of dioscin, Saponins A, B, C, D. Dioscin, Tigogenins. Rhizome: Dioscin, prosapogenins A and B of dioscin, gracillin and beta sitosterol-β-D-glucoside (30). | Kasta, Kasa, Prameha, Sleepada | Sleepada: intake of kebuka kandha (rhizome) juice mixed with bida lavana (Black salt) and juice of *Putranjiva roxburghii* Wall.) relieves filariasis (32). | 1. The Ethanolic extract of the seed containing Saponin produces spasmolytic effect on guinea pig ileum. In Orissa, the rhizome juice with sugar is given internally to treat leprosy. In Andhra Pradesh, the rhizome is used as anti-merin and for abortion. 2. A mixture of saponins from rhizomes shows significant anti-inflammatory, anti-arthritic and anti-fertility activities. 3. The saponins show potent and sustained hypotensive and Brady cardiac activities in dogs with low toxicity and without any Haemolytic activity (33). |
| 2.   | Tala          | *Borassus flabellifer* Linn. / Aracaceae | Male inflorescence: Steroid saponins (borassosides A-f and dioscin), flabelliferrins and a bitter compound of Steroidal Saponins. Spirosterol is a dominant aglycone in the inflorescence (34). | Mutrakricchra, Mutraghata, Amlapitta, Unmada, Visuchi | Mutrakricchra & Mutra vivarnya: Male inflorescence juice mixed with ghee, milk taken in internally relieves the mutrakrichchra (36). | 1. The Ethanolic extract of male inflorescences exhibited significant anti-inflammation activity in acute and chronic inflammation in experimental animals (37). |
| 3.   | Kakamaici     | *Solanum nigrum* Linn. / Solanaceae | Berries: Tigogenins (steroidal saponins), steroidal oligo glycosides (38). | Sotha, Arshas, Kasta, Chardi, Hridroga (39). | Sotha: Fruit is useful in Mutrala and Sotha, Hridroga (40). Kotha (urticarial patches): Shanti is pounded with juice of Kakamachi if applied will alleviate Kotha (41). | 1. Solanum alkaloids have close structural and configurationally relationships with steroidal Sapogenins and many inter conversions between alkaloids and steroids and steroidal Sapogenins have been accomplished. The saponins they are surface active and haemolytic and possess antifungal and cytostatic properties (42). 2. Fresh extract is used for inflammatory swellings, enlargement of liver and spleen and cirrhosis of liver (43). |
| 4.   | Sariva        | *Hemidiscus indicus* Linn. / Apocynaceae | Root: Sarsaponin, Sarsapogenin, Hemidine, Hemidesine (44). Sarsasapogenin contain 3 glucose and one Rhamnose as sugar components (45). | Vrana, Sleepada, Visarpa, Jwara, Prameha, Pradara (46). | Vrana: sariva root alone is capable of cleansing all types of wounds (47). The root is also used as blood purifier, in rheumatism, anti-inflammatory tonic in urinary disorders (48). | A Saponin from it was found to have found to have anti inflammation activity (ICMR, 1968-69) (49). The Ethyl acetate extract exhibited significant anti-inflammatory in both acute and sub-acute methods for inflammation. The plant extracts possesses significant antibacterial and anti-inflammatory properties, also inhibits in vivo, the phagocytosis of the cells of Reticulo endothelial system in mice (50). |
| S.No | Sanskrit name | Scientific name / Family | Part used / Chemical constituents | Indications | Therapeutic uses | Research activity |
|------|---------------|--------------------------|----------------------------------|-------------|-----------------|------------------|
| 5.   | Yastimadhu    | Glycyrrhiza glabra Linn./Fabaceae | Roots, seed: The chief constituent of liquorice is a triterpenoid Saponin known as glycyrrhizin (glycyrrhizic acid) (51). Soyasaponins were isolated from the hypocotyl rootlets and seed. The main chemical constituent of liquorice is glycyrrhizin, a triterpene Saponin with low haemolytic index (52). Liquorice root about 2-12% of glycyrrhizic acid (and a correspondingly larger amount of glyrrhizin, the potassium calcium salt) (53). | Vrana Sotha, Amavata, Chardi, Trishna, Visa, Hridroga (54). | Vrana, Dagdha Vrana: paste of Madhuka and tila mixed with ghee heals Vrana (55). Vata Rakta (gout arthritis): The oil processed from Yastimadhu and Gambari moola is useful in Vata rakta (56). | 1. The liquorice is a mild anti-inflammatory drug for Arthritis and Rheumatism, but causes fluid retention. It is also useful for prevention of infections of urinary tract and for inflammatory skin disorders (57). 2. The saponins can increase antibody production and interferon production (58). 3. Isoliquiritigenin, liquiritigenin, a flavonoid found in liquorice roots. ISL displays antioxidant, anti-inflammatory, antitumor and Hepatoprotective activities (59). |
| 6.   | Dhamargava    | Luffa aegyptica Mill. /Cucurbitaceae | Aerial parts, leaf, seed: Oleanane saponins, lucyoside A-H, leaf contain several triterpenoids along with their saponins, water soluble saponins isolated from seeds (60). | Vrana hara, Sothaghma (61), Kantharoga, Gulma, Udara, Kasa, Rapapitita. | Vrana (all types of ulcers): Patra Swarasa of luffa aegyptica is useful all types of wounds (62). | 1. Sponge gourd extract or saponins (ginsenosides and lucyosides) finds application in a topical medication effective in controlling skin disorders around anus in haemorrhoidal condition (63). 2. The seed possesses significant anti-inflammatory and complement inhibitory activities in adjuvant induced arthritis and carrageenan induced paw edema in rats (64). |
| 7.   | Madhuka       | Madhuka longifolia (Koen.) /Sapotaceae | Fruits, seeds: Saponin, Basianin, Mi Saponin A and B (65). | Visarpahara, Grahani, Daha, Trishna, Swasa, Rapapitita (66). | Visarpa: Madhuka and barley powder mixed with ghee make a paste for external application (67). Kandu &Sotha: Madhuka taila is applied on the skin; it reduces itching and reduces swelling (68). | The kernel contains anti-inflammatory and anti-ulcerogenic saponins, mi saponins A, B, C (bisdesmosides of an olean-12-en-3-ene type Sapogenol of Protobassic acid) (69). |
| 8.   | Brahmi        | Bacopa monnieri (Linn.)/Scrophulariaceae | Whole plant: The plant contains saponins, bacosides A and B, Sapogenins, bacogenins A, A2, A3, A4(Sapogenins) 4 new dammarane type triterpenoid saponins, bacopa saponins A, B, C (70). | Sothahara, Pliharoga - Vridhi, Kasa, Kustha, Pandu, Jvara (71). | Sotha & Amavata: The leaf juice is applied to swellings and as a good liniment for Rheumatism (72). | An n-butanol extract of the plant was analysed and found to contain bacoside A (Bacopa Saponin C). |
| S.No | Sanskrit name | Scientific name / Family | Part used / Chemical constituents | Indications | Therapeutic uses | Research activity |
|------|--------------|--------------------------|-----------------------------------|-------------|-----------------|------------------|
| 8.   | Brahmi       | Bacopa monnieri (Linn.) \ Scrophulariaceae | Whole plant: The plant contains saponins, bacosides A and B, Sapogenins, bacogenins A₁, A₂, A₃, A₄(Sapogenins) 4 new dammarane type triterpenoid saponins, bacopa saponins A, B, C (70). Sothahara, Pliharoga - Vridhhi, Kasa, Kustha, Pandu, Jvara (71). | Sothahara, Pliharoga - Vridhhi, Kasa, Kustha, Pandu, Jvara (71). | Sleepada: The fomentation of whole plant is applied for Elephantiasis (73). | The effects of the *Bacopa monnieri* extract were then studied on morphine induced hyperactivity as well as dopamine and serotonin turnover in the stratum since these parameters have a role in opioid sensitivity and dependence. These findings suggest that nBT-ext BM has an ant dopaminergic \ serotoninergic effect (74). |
| 9.   | Shunti       | Zingiber officinale Roscoe. / Zingiberaceae | Rhizome: α Curcumene, β – D Curcumene, ginger glycolipids A&B, C, gingerone B and C, Saponins etc. (75). | Sotha, Sleepada hara, Hridroga, Swasa, Soola, Anaha, Kasa, Chardi (76). | Amavata: The intake of decoction of Shunti and goskhura relieves Amavata, Katishoda and pains all over the body (77). Kamala (Jaundice): Shunti mixed with jaggery is useful to treat Kamala (78). | 1. It has been reported that an acetone extract of ginger and its fractions were Anti-5-HT (Saponin) effects (79). 2. The Ethanolic extract showed Anti–inflammatory activity in rats. It has shown marked Anti–inflammatory activities in rats which is comparable to prednisolone (80). |
| 10.  | Sigru        | Moringa oleifera Lamk. \ Moringaceae | Seeds: Saponosidique. Whole plant Moringine, moringine, bayrenol, in dolo acetic acid, pterygospermine, carotene etc. (81). | Vidradhi, Sotha, Vrana hara, Galaganda, Apachi, Plee ha (82). | Amavata: Oil of the Seeds with or without the addition of ground nut oil in equal parts is used as an application to relieve the pain of gout and acute rhematism (83). Sotha: Sigru is useful in all types of oedema (84). All parts of the tree are considered medicinal and used in the treatment of ascites, rheumatism, venousomous bites and as cardiae and circulatory stimulations (85). Apachi: Sigru beeja churna nasya is useful in Apachi (86). | 1. The Anti-inflammatory activity is expressed in terms of percentage increase and reduction of edema of the hind paws of mice left by polyphenolic extracts and Saponosidique seeds of *Moringa oleifera*. The Seeds are also used in many parts of India as diuretic for the treatment of oedema, as a febrifuge. The hot aqueous infusion of seeds exhibited Anti - inflammatory, diuretic activities in experimental rats (87). 3. 4 benzyl isothiocyanate 1, 2 isolated from *Moringa oleifera* seeds were screened for their antibacterial activities against staphylococcus aurous, staphylococcus epidermidis, Escherichia coli (88). |
In this study 6 (60%) plants having Sothahara karma, 4 (40%) plants having Vranahara karma, 4 (40%) plants having Sleepada hara karma, 3 (30%) Visarpahara karma, 1 (10%) plant was having mutrakrichchra karma, 4(40%) plant was having Amavatahara karma (Graph No.2).
Discussion

The study was planned to assess the plants mentioned in Ayurvedic classics with anti-inflammatory activity such as Sothahara, Visarpahara, Vranahara, Sleepadahara, Mutrakrichchra hara, Amavatasha etc. which contain steroidal saponins as one of the major phytoconstituent. We have listed out almost 50 plants having saponins as main glycoside, with an anti-inflammatory Pharmacological therapeutic activity. Out of them 10 plants were short listed and tabulated (Table no.1) to brief out. These 10 drugs were classified According to Sothahara, Vranahara, Visarpahara, Sleepadahara, Mutrakrichchra hara, Amavatasha properties as per (Table no.2) also. All these drugs are easily available, highly potent, can be processed easily and echo friendly.

According to Ayurveda Sotha is classified in to 2 types. Sthaniaka (particular part) and sarvadaihika (total body). The above mentioned plants having different karmas, all these karmas are worked on sthanikas Sothaharas. 6 plants having 60% sothaharas, 4 plants having Vranahara 40%, 4 plants having 40% Sleepadaha hara, 3 plants having 30%visarpahara, 1 plant having 10% Mutrakrichchra hara, 4 plants having 40% Amavatasha hara. The highest 60% of sothaharas present.

Conclusion

Based on the studies so far, it can be concluded that saponins hold a lot of therapeutic potential. Along with generalised saponification activity and cell permeability enhancing properties that are interesting, their direct application as anti-inflammatory agent is also useful. It is also important to note that the specificity of anti-inflammatory property must be carefully assessed and tested clinically and pharmacologically for validation, though they are textually recorded.

All the above 10 plants are time tested and mentioned in the classical literature and indicated in many inflammatory disorders with significant rate of success. The study helps to establish a potent drug from the existing formulary.

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