

Anti-acne Phytoconstituents-An intensive Review

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Abstract

In this review an attempt has been made to give a holistic report of the anti -acne phytoconstituents which has been reported possess anti-acne activity in different research work. It was also tried to explain different associated properties of phytoconstituent to analyze the constituents completely. The effort was also made to give the biological sources, family, different constituent and the research work done to identify the vital potential of phytoconstituent which has been utilized or which will be utilized in the development of Ayurvedic anti-acne formulation. Attempt was also made to explain different type of Acne, their causes and pool of information related to them.

Keywords: Phytoconstituents, Antiacne, Potential, Biological Sources, Ayurvedic.

1. Introduction

Skin is the most important and sensitive part of human body. The external environmental exposure leads to many kinds of skin problems and disorders like acne, sunburn and pigmentation⁽²³⁾. Acne is common skin disorder in the age group of 15-25 years due to increased production of sebum followed by the attack of *Propionibacterium acnes*. It usually begins at puberty and worsens during adolescent age, usually early 14-16 years in males and 12-13 years in females. It has been estimated to effect 85% females and 90% males at teenage⁽³⁰⁾. Statistic study revealed that globally. around 3% of adults aged 35-44 years old experienced certain degree of acne, 8% of adult aged 25-34 years old, 85% of young adults aged 12-25 aged old, and in the age of twenty, both men and women continuous suffered by acne with 42.5% and 50.9% respectively⁽²³⁾. Acne leads to significant morbidity that is associated with residual scarring and psychological disturbances such as poor self-image, depression, and anxiety, which leads to a negative impact on quality of life⁽⁷⁾.

1.1 Definition of acne

Acne is a peculiar inflammatory disease associated with sebaceous follicles of skin⁽²⁾, occurs when inflammation or blockage of the hair follicle and their associated sebaceous glands (together known as the pilosebaceous units⁽⁸⁾) attain special conditions (abnormalities in sebum⁽¹⁾ at face, chest, back, scalp, neck⁽²³⁾ and upper arms^(1,2,8,10,15)). It is one of the considerable problem among skin diseases, characterized by scaly red skin (seborrhea),

blackheads and whiteheads (comedones), pinheads (papules), large papules (nodules), pimples and scarring^(1,5). Principally, acne shows an epidermal hyperproliferation that causes follicular hyperkeratosis (comedones- open and closed) that are non-inflammatory lesion and perifollicular inflammation (papules and pustules, nodules, superficial pus and varying degree of scarring) that are inflammatory lesion pathogenic factors includes^(3,7).

Acne is usually caused by increased sebum production influenced by androgen hormone (transient hormonal imbalance in favour of testosterone mainly during puberty in both male and female), altered follicular keratinisation, immune hypersensitivity, oxidative stress, inflammation and bacterial (*Propionibacterium acnes*) colonization^(3,23). Various factors that are involved in the pathogenesis of acne are inter-connected with each other. This disease occurs in both female and male, there is no preference among them but the course is more severe in males⁽¹⁰⁾. The genetic background plays an important role in the severity of acne that varies greatly among individuals⁽⁶⁾. The bacteria *Propionibacterium acnes*, *Staphylococcus epidermidis*, *Staphylococcus aureus*, the fungus *Candida albicans* are almost commonly present in the pustular contents of the acne⁽⁴⁾. *P. acnes* is a Gram-positive, anaerobic, immobile bacterium which has a tendency to colonize in the skin pores and hair follicles. It grows on greasy, sebaceous skin and uses sebum as nutrient source. Sebum plays a role in the pathogenesis of acne, because *P. acnes* releases proteases, hydrolases and lipases into the sebum which promotes oxidative stress, inflammation and tissue destruction⁽³⁾.

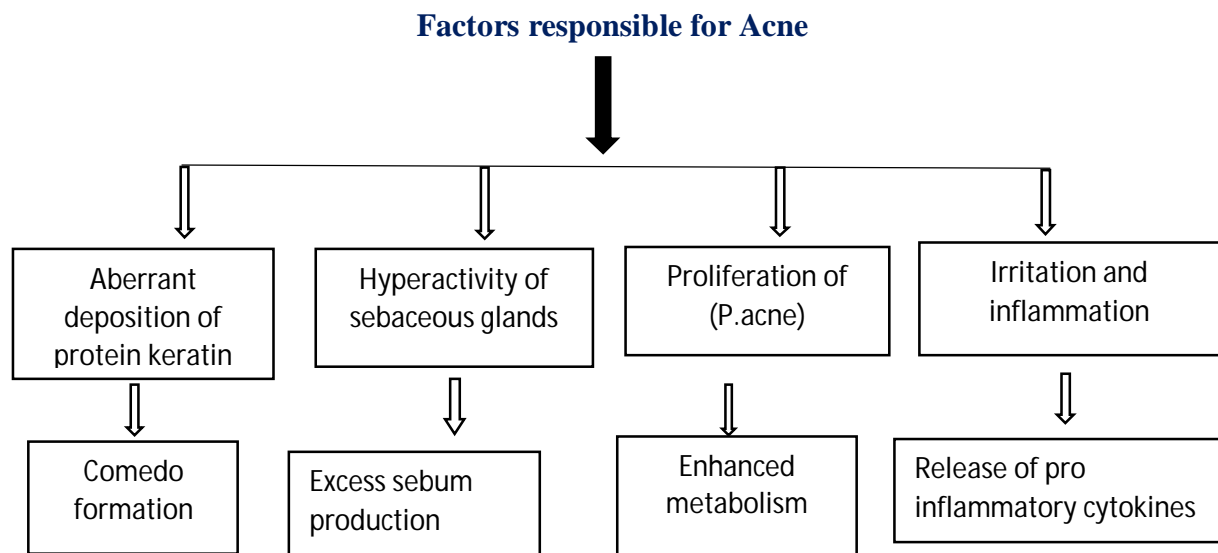


Figure 1. Factors responsible for acne

1.2. Types of acne

1.2.1. Acne vulgaris and acne rosacea

a. Acne vulgaris

The most common form of acne; usually affects people from puberty to young adult hood⁽¹³⁾. It is a human skin disease characterized by the development of seborrhea (red scaly skin),

comedones (black head, whitehead), nodules, papules, pustules and cyst and probably scarring⁽¹⁹⁾. It comes in the areas of the skin that have plentiful hair growth such as in the upper chest, back, legs and face. Sebaceous glands get infected and clogged. Development of several large and small eruptions.

b. Pimple or zit

Pustules or papules are small inflamed elevation of the skin, which are common symptoms in acne. Difference between a pimple and acne: Certain people get one or two spots off and on while others get frequent eruption of spots with lots of pus-filled pimples indicates acne which is a chronic or prolonged condition that affects numerous adults and teens. More or less all human beings in the world gets pimples at some point of time as sooner the body enters into puberty stage at the age of 12, there onset to release hormones and start to function in the bodies of man or woman irrespectively and at this juncture food or pollution, ought to upset hormonal balance thereafter⁽¹³⁾.

“Normal” pimples usually form quickly and then go away again soon afterwards, whereas acne develops over a longer period of time and stays longer. It sometimes leaves small red marks or scars behind⁽²⁰⁾.

c. Acne rosacea, rosacea

Rosacea is a chronic facial inflammatory dermatosis characterized by flushing (or transient facial erythema), persistent central facial erythema, inflammatory papules/pustules, and telangiectasia⁽²¹⁾. rosacea is not primarily a disease of teenagers like common acne but occurs most often in adults (ages 30-50), especially in those with fair skin. It is different than acne, there are usually no blackheads or whiteheads in rosacea. It is a skin disease of adults often affected by women in which blood vessels of the face enlarge indicating a flushed appearance. Rosacea is an adult acne-like skin condition that is common, chronic, and easily controllable and curable medically. Rosacea usually acts upon the central third of the face, especially the nose with periodic stimulation and relief. The symptoms may come and go and the skin may be clear for weeks, months, or years and then may emerge again at a time. Rosacea inclined to develop in certain stages and causes to create inflammation of the skin of the face, especially the forehead, cheeks, nose, as well as chin. Redness of the face, tiny red pimples and fine red lines on the facial skin, an enlarged, bulbous red nose. Eye problems, like swollen, red eyelids and conjunctivitis, these are Symptoms and signs of rosacea⁽¹³⁾. Rosacea can be divided into four subtype- erythemato-telangiectatic, papulopustular, phymatous, and ocular⁽²²⁾.

1.2.2. Types of pimples

Pimples or spots come out when the skin produces much more oil that causes breeding bacteria, which clog the existing pores creating swelling and redness on the skin. Pimples are not at all contagious⁽¹³⁾.

acne as a chronic inflammatory dermatosis which consists of non-inflammatory lesions such as open comedones (blackheads), closed comedones (whiteheads) and inflammatory lesions such as nodules, pustules, papules or reddish papule and cysts^(16, 9, 18). Non-inflammatory acne is a milder type, which most people would refer to as “pimples” or “blackheads” rather than “acne”⁽²⁰⁾.

Among various kinds of pimples, the most common types are mentioned below -

1.2.2.1. Whiteheads- Remain under the surface of skin and are very small⁽¹³⁾. The whitehead (closed comedones) resolves usually within 12 days⁽¹⁷⁾. Whiteheads are closed, and have a white or yellowish head⁽²⁰⁾.

1.2.2.2. Blackheads- Blackheads are small, black bumps that rise to the surface of the skin, often appear on the nose area. open hair follicles clogged with oil cause blackheads. Blackheads look like black spots but do not cause pain, this type of acne is commonly called mild acne because it does not cause inflammation that results in redness of the facial skin⁽²⁴⁾, but are not formed due to dirt⁽¹³⁾. Blackhead (open comedones) resolves over 2-6 weeks. Most of these comedones do not progress to inflammatory lesions⁽¹⁷⁾. Black heads are not black because of dirt they are black in colour. The skin pigment melanin reacts with oxygen that is present in the air. Generally, air oxidises the protein called keratin^(13, 20).

1.2.2.3. Papules - When inflammation is deep, papules are formed, pustules similar to, but with erythema and edema. Papules are clearly seen on the skin. Papules are small tender pink bumps.

1.2.2.4. Pustules- Neutrophils can be added to the surface and cause pustules. Pustules (pimples or zits) are consisting of pus at its top and red at the bottom level can be looked on the surface of the skin, characterized by the appearance of inflammation and pus.

1.2.2.5. Nodules - If there is extensive inflammatory infiltration, the nodules are formed, hot and soft texture and which can be haemorrhagic or suppurative, giving rise to the cysts. Nodules are Clearly visible on the surface of the skin. They are large, painful, solid pimples existing deeply in the skin and can be seen on the skin surface.

1.2.2.6. Cysts -They are deeply rooted, painful and pus filled and easily prone to form scars. They are Clearly visible on the surface of the skin^(11, 13).

1.2.3. Acne vulgaris was graded by Indian tradition using a simple grading system which classified acne vulgaris into four grades as follows⁽⁶⁾.

➤ **Mild (Grade I):** - The mildest form of acne includes comedones - whiteheads (closed clogged pores) and blackheads (clogged pores that are open at the skin surface and more easily noticeable), milia and minor pimples has no inflammation^(6, 19).

- **Moderate acne (Grade II):** - Includes more whiteheads and blackheads plus papules (reddened areas that are elevated above the skin surface) and areas of pustules (pimples—small bumps on the skin that contain visible fluid) in this class of acne. Inflammation is present in comparison to mild acne.
- **Moderate to Severe acne (Grade III):** - This is moderate to severe acne with widespread papules and predominant pustules and nodules^(6, 15). The number of pustules and papules are 40 to 100 with many comedones. Grade III acne displays the redness and inflammation characteristics⁽⁶⁾.
- **Nodulocystic or conglobate severe acne:** - nodules are deeply embedded solid, often painful lesions. These may develop additional infections and may cause widespread scarring if not treated. Nodules can be greater than 5 mm in diameter^(14, 12, 19). People who have severe forms of acne have a lot of pustules and papules, as well as nodules on their skin. These nodules are often reddish and painful⁽²⁰⁾.

1.3. Causes of Acne Vulgaris: - various Causes of Acne

- **Infectious Contribution:** Microorganism like *Propionibacterium acnes* and *Staphylococcus aureus* are one of the causative agents for acne. They are able to adapt the abnormal oil production, inflammation and inadequate sloughing of acne pores.
- **Dietary Involvement:** Acne vulgaris is seen to be associated with foods with having high glycemic index like milk, salt, chocolates etc. The relation of obesity with acne has also shown by studies.
- **Genetic Contribution:** the cause of acne could be genetic rate of acne is seen among first degree relatives and in twin studies as well. The genes attributed to acne, are polymorphisms in IL-1 α , TNF- α and CYP1A1.
- **Hormonal Changes:** Puberty and menstrual cycles, cause hormonal changes, that contributes to acne vulgaris. Androgen is the sex hormone that increase during puberty and pregnancy, could cause the more sebum production in follicular glands. Anabolic steroids can also lead to development of acne vulgaris in adult women⁽⁶⁾.
- **Psychosocial effects of acne:** A correlation between stress and acne severity, stress can induce acne. Additionally, acne itself induces stress and the “picking” of the spots will aggravate the appearance⁽¹⁵⁾.
- **Various other factors:** Smoking and acne, Ultraviolet radiation, Sweating, Premenstrual flare⁽¹⁵⁾.

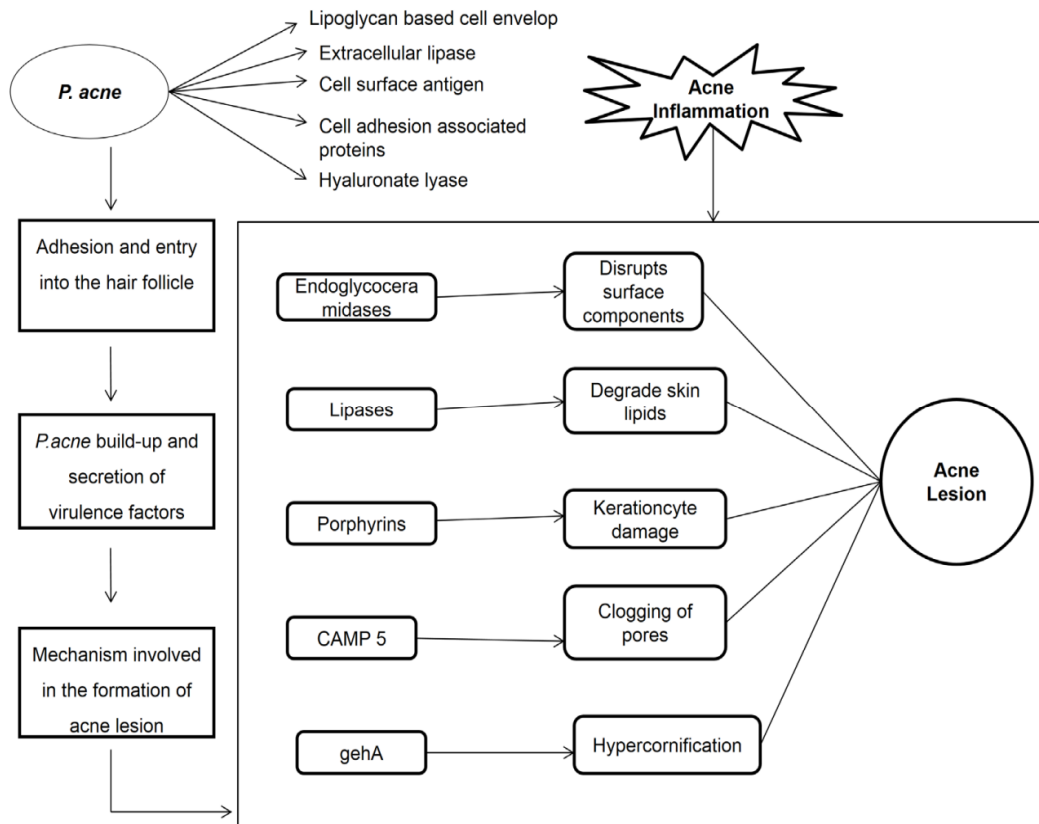


Figure 2. Mechanism of acne formation ⁽⁹⁾

1.4. Pathogenesis of Acne

The pilosebaceous units of the skin presents with a variety of lesions at various inflammatory stages, including acne scars and hyperpigmentation affected by Acne ⁽¹⁶⁾.

The exact mechanism of acne is not known but there are four pathogenic factors.

1.4.1. Increased sebum production

1.4.2. Hypercornification of pilosebaceous ducts

1.4.3. Abnormal bacterial function

1.4.4. Production of inflammation ⁽⁶⁾

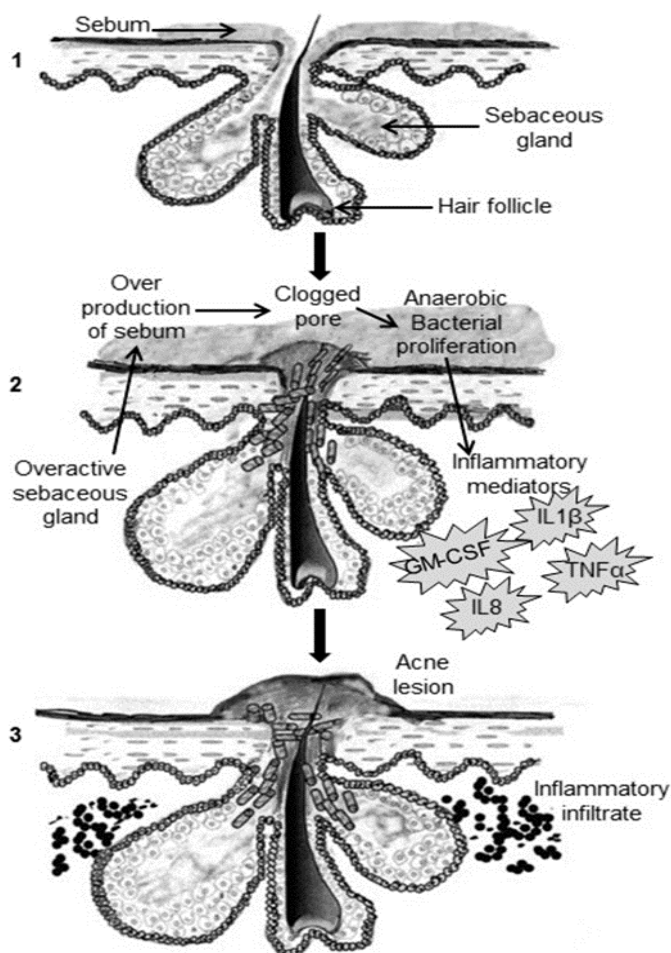


Figure 3. Pathogenesis of acne ⁽¹⁶⁾.

2. Need of Alternative Medicines (Herbal Medicines) in cosmetic industry or cosmeceuticals.

With the history of use from ancient time, Herbal medicines have entered the growing ‘cosmeceutical’ market for combating various skin problems. It is attracting renewed attention even though the mode of action of Phyto-constituents from herbal origin is more complex than mechanisms of one bioactive factor ⁽²³⁾. Natural products are generally used in drug design and drug discovery. Separation of a single entity is very difficult from complex mixture contains fats, oils, alkaloids, tannins, glycoside ⁽²⁵⁾.

Herbal and botanically derived remedies are increasingly popular for the treatment of acne. Many plants are known to have innate antimicrobial and anti-inflammatory properties ⁽²⁶⁾, they are of great utility in cosmetic products for oily, acne prone skin ⁽²⁷⁾. Herbal drugs are traditionally used in various parts of the world to cure a number of ailments ⁽²⁸⁾.

In developing countries, Herbal medicinal preparations are still popular in spite of great advancement in modern medicines in recent decades. Plants are very efficient sources of renewable organic materials such as unusual and nutritionally rich proteins, lipids and

enormous spectrum of chemical constituents. Medicinal plants are known to be much safer. In the world, 5-10% of all plants are systematically investigated for their medicinal property⁽²⁹⁾. In acne treatment, the persistent relevance of antibiotics is coupled with the risk of emerging resistant bacteria. The increase in antibiotic resistance depends on various factors, involving the specific nature of the relationship of bacteria to antibiotics. Occurrence of 250, 000-500, 000 plant species provide a great potential for screening of Phytotherapeutic agents which can be utilized for acne management. Plant derived products offer numerous beneficial effects on the human skin; for example, the capacity of stimulation of collagen and elastin synthesis, the moisturizing effect, strengthening of micro-circulation and skin immunity, anti-inflammatory and anti-microbial effect, as well as certain antioxidant effect due to the capacity to counteract the free radicals produced by solar radiation, aging and pollution. Along with increasing numbers of allergies and side effects to chemical cosmetic ingredients, vegetable extracts and specific phytochemicals have become of high interest in the dermatocosmetic and hygiene product industry⁽²⁷⁾. The traditional bitter herbs may be useful and important for correcting acne vulgaris, by stimulating digestive function, including acid secretion. Herbs with antimicrobial, inflammation modulating, anti-comedogenic, and in certain cases, hormone-balancing actions are also useful for treating acne⁽³⁰⁾.

2.1. Definition of phytoconstituents

According to the world health organization any plant is a medicinal plant, if one or more of its organs contains, substances that can be used for therapeutic purpose, or which are precursors for chemo-therapeutic chemo synthesis. Such a plant will have its parts including leaves, roots, rhizomes, fruits, grains, stems, bark, flowers or seeds, used in control or treatment in a disease condition and therefore contain chemical components that are medically active. These non-nutrient plant chemical compounds or bioactive components are referred as phytochemical or phytoconstituents, and are responsible for protecting the plant against microbial infection and infestations by pests. On the other hand, the study of the natural products is called phytochemistry. The science of application of these indigenous or local medicinal remedies including plants for treatment of diseases is called ethnopharmacology⁽²⁵⁾. Medicinally active portions of medicinal plants are separated from inactive or inert components using selective solvents by standard extraction procedures like decoction, maceration, infusion, digestion, percolation, and soxhlet extraction, because Plant extracts are therapeutically desired. These are obtained in the form of decoctions, infusions, tinctures, semisolids, and powdered extracts⁽⁴⁶⁾.

2.2. Classes of phytoconstituents: alkaloids, Glycosides, Flavonoids, Phenolics, Saponins, Terpenes, Tannins, Anthraquinones, Essential oils, Steroids⁽²⁵⁾.

The aim of the present review is to give all-inclusive information on the Phytoconstituents, pharmacological actions and traditional uses of various genera and species of medicinal plants to explore their therapeutic potential and future research opportunities⁽³¹⁾. These herbal agents possessed not only the antimicrobial activity but they also exhibit the

antioxidant, anti-inflammatory activity. Various Herbs have skin detoxifying property which is considered as good source for the treatment of acne. There are some Indian medicinal plants used in the treatment of acne vulgaris that are listed below⁽²³⁾.

3. *Moringa oleifera* Lam

Enormous number of medicinal plants have been recognized as valuable sources for such natural antimicrobial compounds, and One such species is *M. oleifera* Lam. belong to the family Moringaceae, a monotypic of single genera with around 33 species of which 4 are accepted, 4 are synonym and 25 have not been assessed⁽³⁵⁾. *Moringa oleifera* (the sole genus)⁽³²⁾ or Sahijan also called Drumstick tree or Horseradish tree⁽⁴⁰⁾ is a fast-growing softwood tree indigenous to sub-Himalayan tracts of Northern India. Nowadays, *M. oleifera* is mainly found in African and Asian countries and in Middle East, but, due to its adaptability, it is spreading to other areas, especially tropical and subtropical lands affected by drought⁽³³⁾.

Thirteen species such as *M. oleifera*, *M. borziana*, *M. rivae*, *M. peregrine*, *M. concanensis*, *M. longituba*, *M. hildebrandti*, *M. arborea*, *M. pygmaea*, *M. ovalifolia*, *M. drouhardii*, *M. stenopetala* and *M. ruspoliana* are reported in the genus of *Moringa*, yet, among which *M. oleifera* is the most known for its rich nutrients⁽³¹⁾.

3.1. Part of plant

Traditionally, the young capsules, seeds, leaves, fruits, flowers and immature pods and roots of this plant are edible^(34,39).

3.2. Phytoconstituents

M. oleifera consists of 539 bio-chemical activities which are much more beneficial to human being⁽³¹⁾. *Moringa oleifera* L. leaves contain flavonoid, alkaloid, and phenolic compounds which have antibacterial activity Against staphylococcus epidermidis bacteria that causes acne⁽³⁸⁾. Different parts of the MO tree have been established as being good sources of unique glucosinolates, and flavonoids phenolic acids, tocopherols ascorbates, beta-sitosterol, moringine, polyunsaturated fatty acids (PUFAs), highly bioavailable minerals. The most predominant is Glucomoringin {4-O-(α -L-rhamnopyranosyloxy)-benzylglucosinolate} in the flowers, pods, stem, leaves and seeds of *M. oleifera* among glycosinolates^(34,36). The leaves, which are rich in protein (27%), and are rich in vitamins A, B1, B2, B3, and C, calcium, iron and phosphorus, Magnesium minerals, polyphenols, phenolic acids, flavonoids, alkaloids, glucosinolates, isothiocyanates, tannins and saponins, β -carotene and antioxidant compounds, are used not only for human and animal nutrition but also in traditional medicine. *Moringa* leaves have the vitamin C content of 7 oranges, calcium equivalent of 4 glasses of milk, potassium of 3 bananas, 3 times the iron of spinach, 4 times the amount of vitamin A in carrots, and 2 times the protein in milk^(32,40). The MO leaves are a rich source of omega-3 (α -3) and omega-6 (α -6) polyunsaturated fatty acids (PUFAs), in the form of α -linolenic acid (C18:3, α -3, 49-59 %), and linoleic acid (C18:2, α -6, 6-13 %). In the *Moringa* leaves,

Palmitic acid (C16:0) is the major saturated fatty acid, accounting for 16-18 % of the total fatty acids ⁽³⁶⁾. Along with Moringa oil, the seed has a high protein content, on average 31.4%, whereas carbohydrate, fibre and ash contents are 18.4%, 7.3% and 6.2%, respectively ⁽³³⁾. *M. oleifera* seed kernels, contain a significant amount of oil (up to 40%) with a high-quality fatty acid composition (oleic acid > 70%) and a notable resistance to oxidative degradation, after refining, and due to these characteristics, seeds have attracted scientific interest in the form of *M. oleifera* seed. Commercially, the oil is known as “Ben oil” or “Behen oil” ⁽³³⁾. Pterygospermin, a compound found in the flowers and roots of the moringa tree, has powerful antibiotic and fungicidal effects ⁽⁴⁰⁾. Three isomers of 4-*O*- (α -L-acetyl rhamnopyrosyloxy)-benzyl glucosinolate were also found out in *M. oleifera* leaves, depending on the maturity and physiological properties of the leave ⁽³⁷⁾.

3.3. Uses: The multiple biological activities

Moringa leaf extract showed an antibacterial activity against *Propionibacterium acne* and ethanolic extract of Moringa leaves with specific concentrations (5%, 10%, and 15%) has strong inhibitory activity against *Staphylococcus aureus* in ointment preparations ⁽³⁸⁾.

The phytochemicals of MO have shown antinociceptive, anti-atherosclerotic, anti-dyslipidemic, anthelmintic, antihyperglycemic, anti-inflammatory, antimicrobial, antioxidant, antiproliferative, anti-ulcer, antiperoxidative, cardioprotective, antiurolithiatic, and hepatoprotective properties, antifungal, antibacterial. Potent antiproliferative and apoptotic properties of the MO leaf extract ^(36,39). The fruit (pods), flowers, seed, roots, bark, gum, leaf and seed oil of MO have various biological activities, including protection against gastric ulcer, antidiabetic, hypotensive and anti-inflammatory effects. MO leaves have been used for the treatment of various diseases from malaria and typhoid fever to hypertension and diabetes ⁽³²⁾. Moringa leaves are empirically known has an antibacterial activity, because Moringa leaves contain secondary metabolites such as flavonoids, alkaloids, and phenols ⁽³⁸⁾. MO leaves also protect against oxidative stress, inflammation, hepatic fibrosis, liver damage, bacterial activity, cancer and liver injury, strongly inhibiting the growth of *Staphylococcus aureus*, *Salmonella typhi*, *Shigella* species and *Candida albicans* ^(39, 32). MO is grown for its nutritious pods, edible leaves and flowers and can be utilized as food, medicine, cosmetic oil or forage for livestock ⁽³²⁾. Moringa oil properties make it suitable for both human consumption and commercial purposes like biodiesel, cosmetics, and a lubricant for fine machinery ⁽³³⁾. Recently, isothiocyanates of Moringa have become a major research interest because of their various biological activities such as their anticancer, antidiabetic, antimicrobial, and anti-inflammatory effect ⁽³⁷⁾.

4. *Rubia cordifolia*

Rubia cordifolia commonly known as Indian Maddar and Manjishtha in Sanskrit. It is belonging to family Rubiaceae. Drug consists of dried root and stem and is distributed in the Himalayas and other hilly districts of India ⁽⁴²⁾.

4.1. Chemical constituents

The roots and stems of this plant are well known source of Anthraquinones, Several compounds like alizarin, 1-hydroxy-2-methyl-9, 10-anthraquinone, 1, 3, 6-trihydroxy-2-methyl-9, 10-anthraquinone-3-O-(6'-O-acetyl)-alpha-L-rhamnosyl(1-2)-beta-D-glucoside, 1, 3, 6-trihydroxy-2-methyl-9, 10-anthraquinone-3-O-alpha-L-rhamnosyl (1-2)-beta-D-glucoside, 1, 3, 6-trihydroxy-2-methyl-9, 10-anthraquinone-3-O-(6'-O-acetyl)-beta-D-glucoside, 2-carbomethoxy-3-prenyl-1, 4-naphthohydroquinone di-beta-D-glucoside, rubimallin, beta sitosterol and daucosterol are isolated from the root of *Rubia cordifolia* and their structures are spectroscopically proven and contain potent anti-inflammatory activity while 1, 3, 6-trihydroxy-2-methyl-9, 10-anthraquinone-3-O-(6'-O-acetyl)-alpha-L-rhamnosyl (1-2)-beta-D-glucoside, beta-sitosterol and daucosterol contain antibacterial activity⁽⁴³⁾. Rubiacordone A, rubiadin and Hydroxyanthraquinones showed antimicrobial and antioxidant activity⁽⁴¹⁾.

4.2. Uses

Despite the traditional use of *Rubia cordifolia* plant, some studies have reported for its anti-oxidative, and anti-inflammatory, antibacterial, anticonvulsant activities. Since the oxidative stress, enteric pathogen infection, deranged intestinal motility are the established etiopathology of diarrhea⁽⁴⁴⁾. *Rubia cordifolia* is used to manage dropsy, paralysis, amenorrhea and jaundice. In Chinese Medicine, the root of the *Rubia cordifolia* can stop bleeding, promote blood circulation to remove blood stasis and is commonly used to treat arthritis, hematorrhea, haemostasis and dysmenorrhea⁽⁴⁴⁾.

One of unique action of its root is anti-acne effect through anti-inflammatory, anti-oxidant⁽²³⁾, anti-bacterial, and anti-androgen action. The roots have also been reported an antioxidant, anti-inflammatory, anticancer, immunomodulator and hepatoprotective and are extensively used against blood, urinary and skin diseases. Manjishtha is reputed as an efficient blood purifier and hence is extensively used against blood, skin and urinary diseases in ancient world. It remained a potent drug for obstinate skin diseases, erysipelas, leucoderma and oedema also used as febrifuge and against blood disorders in Ayurveda⁽⁴¹⁾. Manjishtha is applied Externally on major burns, mixed with honey on freckles and blemishes⁽⁴⁵⁾.

5. *Eugenia caryophyllata*

Eugenia caryophyllata also sometimes *Syzygium aromaticum* Linn or Cloves are an unopened⁽⁴⁷⁾ aromatic dried flower⁽⁴⁸⁾ buds of a tree belongs to the family Myrtaceae⁽⁴⁹⁾, which is same as that of guavas⁽⁴⁷⁾. It is used as a spice in virtually all the world's cuisine. The term 'Clove' is derived from the English word 'Clout' and the French word 'Clou' and both meaning 'nail'-from the likeness of the flower bud of the Clove tree to a broad headed nail⁽⁴⁾. Clove (*Syzygium aromaticum* Linn) belongs to the family Myrtaceae with aromatic dried flower buds⁽⁴⁹⁾. Cloves are the dried flower buds of clove tree, *Syzygium aromaticum* (synonym: *Eugenia caryophyllata*)⁽⁴⁸⁾.

5.1. Pharmacological properties

Clove oil has been revealed with various pharmacological and biological properties such as anaesthetic, analgesic effects as well as anti-microbial, antioxidant, anti-inflammatory, anti-carcinogenic, anti-mutagenic, anti-convulsant and neuro-protective activities⁽⁴⁸⁾. According to previous studies eugenol exhibits anti-inflammatory, anti-bacterial, anti-oxidative and neuro-protective activities⁽⁴⁸⁾.

5.2. Phytoconstituents

Clove contains 15-20% essential oil, 6-7% non-essential ether extract, 10% fixed oil, and 10%-13% tannin (gallotannic acid), eugenin, besides glycosides and flavonols. The essential oil of Clove bud contains caryophyllene, eugenol acetate (2-17%) and eugenol (about 70-90%), as its main constituents⁽⁴⁾. Eugenol (4-allyl-2-methoxyphenol) is the chief component that exists in clove essential oil with high antimicrobial, antioxidant, and insecticidal activities, is commonly used as a flavouring agent in cosmetics and food products and, in particular, in zinc oxide eugenol chelating cement in dentistry^(49, 47, 48). The dried dark and flower buds also contain nutrients like proteins, cellulose, pentosans, minerals, vitamins, resins, carbohydrates etc.⁽⁴⁾. In India, Clove buds contained 12.9-18.5% oil, of which 44-55% is eugenol, whereas the pedicels contained 3.0-7.7% oil with 60.0-72.4% eugenol. Cloveleaf and bud oil contain various classes of compounds e.g. monoterpenes, sesquiterpenes, aldehydes and ketones⁽⁴⁷⁾. Other substances present in traces are methyl furfural, dimethyl furfural, α -pinene, methyl-n-heptyl ketone, furfural, methyl-n-amyl carbinol (2-heptanol), methyl salicylate, methyl benzoate, methyl alcohol, benzyl alcohol, methyl-n-heptyl carbinol and vanillin⁽⁴⁾.

5.3. Uses

Clove has been added to foods not only as a flavouring agent, but also as a preservative due to its Eugenol content, acts as a preservative in food to prevent food borne pathogens and spoilages⁽⁴⁹⁾ its anti-oxidant and anti-bacterial properties. In Chinese traditional medicine, clove is used to treat dyspepsia, acute/chronic gastritis and diarrhea⁽⁴⁸⁾. Clove oil is used in aromatherapy and is successfully used for asthma and various allergic disorders by oral administration⁽⁴⁾. Indonesia uses half the world production of cloves to make kretek cigarettes in the proportion of one part of clove mixed with two parts of tobacco. Clove cigarettes were banned in the U.S. In 2009, however they are still marketed with the new label as filtered clove cigars⁽⁴⁷⁾. The oil is used in perfumery, in the manufacture of vanillin, and as a general antiseptic in medical dental practices. Externally Clove oil is used as a rubefacient and counterirritant. Despite these properties, the common spice Clove is not popular in cosmetics, may be because of inadequate scientific evidence to support the claims made about the various properties of the Clove oil in cosmetic preparations⁽⁴⁾. In recent years, a large number of essential oils and their constituents have been investigated for their antimicrobial properties against some bacteria and fungi. It is reported that essential oils

provide a gentle and inexpensive way of treating acne, clearing infections and healing acne scarring⁽⁴⁾.

6. Myristica Fragrans Houtt.

Myristica fragrans Houtt. From family Myristicaceae (A family of flowering plants indigenous to Asia, Africa, Pacific Island, and America) is a bushy evergreen tree about 10-20m in height, indigenous to India, Indonesia, Sri Lanka Pacific Island and America. Nutmeg is a common fruit/seed of plant origin drug *Myristica fragrans* Houtt. used as spices as well as for medicinal purpose in Unani and Ayurveda System of Medicine since antiquity and presently, with growing evidence still maintains its status as a unique kitchen spice for many of its traditional uses as a natural remedy. East Indian nutmeg is available in three grades; Banda Nutmeg, containing up to 8% essential oil and consider to be the finest for use, Siauw nutmeg is almost as good as Banda, it containing 6.5% essential oil and Penang Nutmeg, which is usually wormy and moldy and suitable only for distillation purposes^(50, 51, 52). Numerous other species of *Myristica* besides *M. fragrans*, are grown all over the tropical regions including *M. malabarica* and *M. beddomeii* (Indian), *M. argentea*, and *M. fatua* and has been known by most taxonomists^(52, 55). Bombay nutmeg is obtained from *Myristica malabarica*, and *M. malabarica* is used to adulterate true nutmeg^(51, 53). The material is molded into shape and sometimes used as an adulterant of true nutmeg is known as Fictitious nutmeg. It is controversial that Papu nutmeg is derived not from *M. fragrance* but from the allied species *Myristica argentea* Warb.; it is sometimes classed as the fourth grade of East Indian nutmeg and can be disguised from the true nutmeg⁽⁵¹⁾.

6.1. Phytoconstituents

Principal constituents of nutmeg are fixed oil (25-50% lipids as fixed oil mainly of myristic, petroselinic, and palmitic acids), the major component of fixed oil is trimyristin, volatile oil (Myristicin; 4-methoxy-6-(2-propenyl)-1, 3-benzodioxole is a major compound of the essential oil of seeds and mace nutmeg) and starch and nutmeg butter from its bark and leaves^(51, 57, 56). Nutmeg butter (extracted fixed oil) mainly contains saturated fats (90%) with 10% unsaturated fats. Nutmeg contains 74.9% myristic acid of total lipids that is 35.7%. The constituents of nutmeg can be broadly classified into phenolic acids, terpenoids, fatty acids, lignans, neolignans and miscellaneous compounds. Nutmeg contains moisture, 14.3%; protein, 7.5%; carbohydrates, 28.5%; fiber, 11.6%; ether extract, 36.4%; and mineral matter, 1.7%; phosphorus, 0.24%; calcium, 0.12%; and iron, 4.6 mg/100 g, resins, proteins, cellulose, magnesium and potassium. It contains volatile oil (6-16%), starch (14.6-24.2%), pentosans (2.25%), furfural (1.5%), and pectin (0.5-0.6%). It is a fair source of vitamins⁽⁵¹⁾. The kernel (*Myristica fragrans* seed) consists of 30-55% oil and 45-60% solid matter, the volatile oil accounts for 5-15% of the nutmeg kernel, while the fixed oil accounts for 24-40%⁽⁵⁵⁾.

The essential oil of nutmeg mainly contains terpenes; sabinene (15-50%), α -pinene (10-22%) and β -pinene (7-18%) with myrcene (0.7-3%), γ -terpinene (3.9%), camphene (0.3%), p-

cymene (0.7%), terpene derivatives; linalool (0.8%), 2-terpinen-4-ol (0-11%), geraniol, Phenylpropanes; safrole (0.1-3.2%), elemicin (2.4%), myristicin (0.5-13.5%), 1, 8-cineole (1.5-3.5%), limonene (2.7-4.1%), α -thujene (2.2%), and,), α -phellandrene (0.7%), δ -3-carene (0.8%), α -terpinene (2.2 %), 1, 8 cineol+ β -phellandrene (2.3%), terpinolene (1.2%), (Z)-P-menth-2-en-1-ol (0.4%), trans-sabinene hydrate (0.5%), (E)-P-menth-2-en-1-ol (0.3%), α -terpineol (0.6%), eugenol (0.4%), methyeugenol (1.6%), β -caryophyllene (0.2%), β -cubebene (0.1%), trans-methyl isoeugenol (0.2%), trans- α -bergamotene (0.1%), germacrene D (0.1%), and Oils consist 85-93% monoterpene hydrocarbons, 6.6-12% oxygenated monoterpenes and sesquiterpenes, and 3.5% aromatic ethers. The composition of nutmeg seed oil depends upon its source^(50, 51, 52, 54).

The predominant leaf oil of Nutmeg is monoterpenes. The leaves of *M. fragrans* Houtt. yield 0.5-2.0% volatile oil. Elemicin and Myristicin are present in the oil of the nut, mace, and leaves. The chief components of the Nutmeg flowers oil are sabinene, pinene, α -terpineol, terpinen-4-ol, and elemicin⁽⁵¹⁾.

6.2. Pharmacological properties

6.2.1. Antimicrobial activity

Nutmeg oil reveals a strong antibacterial activity against 25 genera of bacteria. Camphene presents in the oil that has strong antibacterial, antifungal, and insecticidal properties. The extract of nutmeg has a strong antibacterial activity against non-pathogenic and pathogenic *E. coli*, but the strain O157 showed more sensitive to β -pinene than non-pathogenic *E. coli* strains. The chloroform extract of seed showed a potent antibacterial activity against Gram-positive and Gram-negative bacteria. Trimyrustin and myristic acid also showed good antibacterial activity that was isolated from the extract⁽⁵¹⁾.

6.2.2. Antifungal activity

Myristica fragrans seed Extract with methanol have strong antifungal activity in vitro and in vivo against numerous plant pathogens. From the methanol extract, the three lignans isolated, namely, erythro-austrobailignan-6 (EA6), meso-dihydroguaiaretic acid, and nectandrin-B (NB), showed varied antimicrobial activity on the target species. The potentials of essential oil and acetone extract of nutmeg as antifungal, antibacterial, and antioxidant were carried out by different techniques. Antifungal activity of essential oil from nutmeg reported by Rahman *et al.*⁽⁵¹⁾.

6.2.3.1. Antioxidant Activity

A stronger antioxidant activity showed by aglycone fraction from glycosidically bound volatiles of nutmeg compared with free volatiles from its essential oil. Higher antioxidant activity of nutmeg oil is reported at 180°C. An ingredient of nutmeg is Eugenol (allylbenzene), inhibits the accumulation of lipid peroxidation products in red blood cells and maintains the antioxidant enzymatic activities such as superoxide dismutase, glutathione

peroxidase, catalase, glutathione-S-transferase(s), glutathione reductase, and glucose-6-phosphate dehydrogenase at normal levels ⁽⁵¹⁾. Antibacterial activity, Insecticidal and repellent activity, Anti-amoebic activity, Hypolipidemic activity, Anticancer activity, Aphrodisiac activity, Anxiogenic, analgesic and sedative activities, Antidepressant activity, Anti-inflammatory activity, Hepatoprotective activity, Anticonvulsant activity, Anticariogenic activity, Antidiarrheal activity, Antiplatelet activity ⁽⁵¹⁾.

6.3. Uses

It is used for fragrances and as a spice in various dishes, as components of tea and soft drinks or mixed in milk and alcohol. Nutmeg is sometimes used as a stomachic, stimulant, carminative as well as for intestinal catarrh and colic in traditional medicine, to stimulate appetite, to control flatulence, and it has a reputation as an emmenagogue and abortifacient. M. fragrans also possess for antiparasitic abilities, anticarcinogenic, anti-papillomagenic, anti-inflammatory activity, antidiabetic, hepatoprotective and excellent antibacterial properties, astringent, hypolipidaemic, antithrombotic, antiplatelets total, antifungal, treatment of dyspepsia, muscle and joint weakness, kidney stone, digestion, increase blood circulation, respiration, liver detoxification, and some reviews stated, that chemically synthesized compound of *Myristica fragrans* has been deductively approved to treat hypolipidemic and hypocholesterolemic, antidepressant, aphrodisiac, antimicrobial, upper antioxidant, memory-boosting, and hepatoprotective properties ^(52, 58, 56).

7. Glycyrrhiza glabra Linn

Glycyrrhiza glabra Linn. commonly known as liquorice (mulethi), belonging to Fabaceae family (also known as Leguminosae) is a perennial herb or undershrub that is about 1 m high. Its dried peeled or unpeeled underground stems and roots constitute the drug, used by various cultures for thousands of years to relieve coughs, sore throats, and gastric inflammation (in all catarrh and cough syrups, pastilles and throat lozenges). The roots and rhizomes are the chief medicinal parts of Licorice. *Glycyrrhiza* includes around 30 various species consisting *G. glabra*, *G. uralensis*, *G. inflata*, *G. eurycarpa*, *G. aspera*, and *G. korshinskyi*. *Glycyrrhiza uralensis* Fisch, *Glycyrrhiza inflata* Bat. and *Glycyrrhiza glabra* L. were prescribed as licorice (in Chinese pharmacopoeia). Its use as a remedy for ulcers and quenching of thirst mentioned by Hippocrates (400 BC). The FDA also lists liquorice as GRAS (generally regarded as safe) when used as food flavouring and sweetening agent. It is grown in some parts of India and has been used extensively over the centuries for sore throat and cough. The previous study indicate that liquorice is safe, well accepted among child patients ^(64,60,62,59,66). This species is a native of Mediterranean areas, but it is now also present in India, Russia, and China ⁽⁶⁰⁾.

7.1 Phytoconstituents

Nearly 300 flavonoids and More than 20 triterpenoids have been isolated from liquorice. Among them, liquiritigenin (LTG), licochalcone A (LCA), glycyrrhizin (GL), 18 β -glycyrrhetic acid (GA), licochalcone E (LCE) and glabridin (GLD) are the main active

components which possess antiviral and antimicrobial, anti-inflammatory and antioxidant activities. 73 bioactive components and 91 potential targets have been identified to date among the components which are isolated from licorice. Licorice contains a variety of nutrient substances such as sugars up to 18%, flavonoids, saponoids, amino acids, asparagine, sterols, mineral salts (such as calcium, phosphorus, sodium, potassium, iron, magnesium, silicon, selenium, manganese, zinc and copper), pectins, resins, gums, starch and Oestrogens, tannins, phytosterols (sitosterol and stigmasterol), coumarins, vitamins (B1, B2, B3, B5, E and C) have been reported. GL (A triterpenoid glycoside which constitutes up to 14% of total soluble solids content or a mixture of potassium-calcium-magnesium salts of glycyrrhizic acid and one of the major compounds isolated from the roots of Licorice)^(61, 59, 67, 63). The liquorice saponins are present in the form of glucuronides, whereas the aglycones are in the form of oleananes. The triterpene saponins being responsible for the sweet taste as a major characteristic constituent⁽⁶⁰⁾.

In recent years, many studies have shown that liquorice aqueous extract, ethanol extract and supercritical fluid extract have potent effects in inhibiting the activities of Gram-positive bacteria and Gram-negative bacteria, such as *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Escherichia coli*, *Candida albicans* and *Bacillus subtilis*. As potential alternatives, these extracts are also being considered to synthetic fungicides, or as lead compounds for new classes of synthetic fungicides. On the basis of above inhibitory activities against bacteria, licorice may serve as an alternative therapy for treating periodontal disease, digestive anabrosis, tuberculosis and dental caries⁽⁵⁹⁾.

7.2 Uses

The secondary metabolites of this plant have been used in relieving respiratory ailments (such as bronchitis, allergies, cold, tuberculosis, and sore throats), their demulcent effect (soothing, coating agent), relieving stomach burn symptoms including heartburn resulting from reflux or any other cause, and treating gastritis, inflammatory disorders, liver problems, and skin diseases, petroleum extract of *Glycyrrhiza glabra* promotes hair grow. The licorice roots have antiulcer, expectorant, diuretic, laxative, sedative, antipyretic, antimicrobial, anti-inflammatory, antioxidant, significant antitumor activity, memory enhancement effect and anxiolytic activities, skin eruptions including dermatitis, eczema, pruritus and cysts, antiseptic activity, hypocholesterolemic and hypoglycemic, preliminary free radical scavenging. The liquorice can also be applicable in the management of impaired learning, Alzheimer's disease, dementia and other neurodegenerative disorders. Skin depigmenting, antiaging, skin whitening and anti-erythemic activities, an emollient, an antiacne activity, a potential cancer chemo-preventive agent, cardioprotective effects, restoring liver function in patients suffering from hepatitis C, hepato protective, antidepression and atherosclerosis and photoprotection effects could be mainly provided by using licorice extract⁽⁶³⁾. The chief ingredient in the hydrophobic fraction of licorice extract is Glabridin, which inhibits tyrosinase activity in B16 murine melanoma cells. Other active compounds, such as isoliquiritigenin, licuraside, glabrene, isoliquiritin and licochalcone A, isolated from licorice

extracts, also shown to inhibit tyrosinase activity. Liquiritin has no effect on tyrosinase, it causes depigmentation by other mechanisms^(67, 68, 65).

In traditional Chinese medicine, the plant is recommended as a common remedy for gastrointestinal problems, cough, bronchitis and arthritis. In particular, it is widely used to treat gastritis, peptic ulcers, respiratory infections, and tremors in folk medicine. Commonly, *G. glabra* root is used in tea that is an excellent thirst quencher. Dried root used as a tooth cleanser, the most important industrial use of *G. glabra* is the production of food additives, such as flavours and sweetening agents (as a flavouring agent for American-type tobacco, chewing gum, candies, baked goods, ice cream, and soft drinks) and to mask the bitter taste in medicinal preparations. In beers and fire extinguishers, the root extracts are used as foaming agents, whereas the root fibers are used in insulation, wallboard, and boxboard materials, after removal of the medicinal and flavouring constituents. In the cosmetic field, *G. glabra* is used as a skin depigmentation agent and is being incorporated in topical products⁽⁶⁰⁾. Health products that contain licorice include herbal and licorice-flavoured cough mixtures, throat pearls, licorice tea, licorice-flavoured diet gum, laxatives (including cascara and compound licorice powder)⁽⁶¹⁾.

Table 1. Different Natural phytoconstituents used in the development of Antiacne formulation (end of the paper)

Conclusion

The intense study of phytoconstituents used in anti-acne purpose revealed that phytoconstituents have tremendous potential to treat skin problems like acne. This is the most safe, reliable way to get rid of acne and most effective way. In this review it was also tried to summarize causes, plant sources, their constituents and utility of these constituents have been exhibited. In a nutshell it could be concluded that nature has all the treatment of ailment, the need is to discover it, formulate it and utilize it in proper manner.

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Table 1. Different Natural phytoconstituents used in the development of Antiacne formulation

S. N.	Biological source	Part of plant	Active constituents	Market products	Company name
1.	Moringa oleifera Lam.	Leaves, seed (37)	4-O-(α -L-rhamnopyranosyloxy) benzylglucosinolate (glucomoringin (GMG), 4-[4'-O-acetyl- α -L-rhamnosyloxy) benzyl] isothiocyanate (31), Gallic acid, Salicylic acid, Gentisic acid (37), Benzylglucosinolate (glucotropeolin), (41, Quercetin, Niazimicin, Rutin (37), quercetin, kaempferol (36), Pterygospermin(39).	1. Rks Aroma Moringa Cream (amazon.in/Rks-Aroma-Moringa-Cream-50) 2. Sunlite spray (Clearance sale) (Amazon.In/Aroma-magic-sunlite-spray-100M) Moringa skintoner (aromamagic.com/products/moringa-skin-toner) 4. Natural Radiance Day Cream (mamaearth.in/product/mamaearth-natural-radiance-day-cream)	Rks Aroma, Aromamagic, RksAroma, Mamaearth.
2.	Rubia cordifolia Linn.	Root (23)	Hydroxyanthraquinones, Rubiacordone A, rubiadin, Sitosterol and Daucosterol, Aldehydeacetate, dihydromollugin, rubimallin (41, 43).	Aroma Magic anti pigmentation glossy pack (amazon.in/ aroma-magic-anti-pigmentation-glossy) Divyakantilep (patanjaliayurved.net/products/ ayurvedic-medicine)	Aromamagic, Patanjali.
3.	Eugenia caryophyllata	leaves, stem, buds* and fruit (47)	Eugenol, eugenylAcetate, β -caryophyllene (4, 47).	Aroma Magic anti pigmentation glossy pack (amazon.in/ aroma-magic-anti-pigmentation-glossy) Neem & Clove Ultra-Purifying Face Wash (lotuserbals.com/products/neemwash-neem-clove-ultra-purifying-face-wash)	Aroma magic, Lotuserbals

4.	Myristica Fragrans Houtt.	Seed (nut) oil, mace (51).	Trimyristin and myristic acid, camphene, macelignan, Eugenol, Lignans-EA6, MDA and NB, sabinene, Essential oil (51).	Aroma Magic anti pigmentation glossy pack (amazon.in/ aroma-magic-anti-pigmentation- glossy) Divyakanti lep (patanjaliayurved.net/ products/ayurvedic-medicine)	Aromamagic, patanjali,
5.	<i>Glycyrrhiza glabra</i> Linn	Root (68), Rhizomes (23)	Flavonoid, saponin (23), Glycyrrhizin, licochalconeA, Glabridin, licoricidin, coumarin derivative (68), Liquiritin (65)	(himalayawellness.in/products/himalaya- men-power-glow-licorice-face -wash) Skin lightening serum (aromamagic.com/products/skin-lightening- serum)	Himalaya herbal, Aromamagic