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Review Article

Herbal cosmeceuticals: New opportunities in cosmetology

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ABSTRACT

Cosmeceuticals are defined as cosmetic products designed to improve and enhance the physical appearance, beauty, health as well as treat the skin ailments. The main objective of the present review is to document various plants along with their active phytochemicals like alkaloids, flavonoids, saponins, sterols, triterpenes, tannins, etc. responsible for activities like antioxidant, anti-inflammatory, sunlight protection, skin regeneration, de-pigmentation, anti-dandruff, anti-hair fall, anti-lice, etc. This study also provides an overview of geographical distribution, environmental attributes, extraction and isolation procedure of active phytochemicals responsible for biological activity. This review further tries to assess the regulatory scenario of cosmeceuticals as they are placed under the subclass of cosmetics under Europe and Japan regulations , whereas in US regulations, cosmeceuticals are placed under the subclass of drugs. The application of nanotechnology in formulating cosmeceuticals (nano-cosmeceuticals) has also seen the light of the day. It can be viewed as a "new paradigm" in the cosmetic industry.

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1. Introduction

he concept of cosmeceuticals was first created by Raymond Reed, founder of the U.S. society of cosmetic chemist and was further popularised by Albert Klingman, American dermatologist. Cosmeceuticals are the advances made within the field of skin care and hair care products (Kumar, 2017). Cosmeceuticals thus, defined as ingredients that exhibit cosmetic activities along with therapeutic and healing properties, hence forth, acting as a bridge between care products that cleanse and beautify and pharmaceuticals that cure and heal (Bellad, 2017). Active cosmetics, nutricosmetics and dermaceuticals are the various terminologies used in place of cosmeceuticals. Herbal cosmeceuticals have gained enormous popularity among the population of both rural and urban areas due to enhanced efficacy, intrinsic acceptability in routine life and reduction of side effects which are commonly observed in synthetic products (Kumar, 2017). The various phytochemicals responsible for exerting cosmetic and therapeutic activities were flavonoids, alkaloids, saponins, sterols, essential oil, tannins, vitamins and trace minerals (Mishra and Mishra, 2016).

As botanicals contain numerous phytochemicals within, the first step involved in the preparation of herbal cosmeceuticals is the identification of the source of phytochemicals. Afterwards, the extraction of chemicals is performed. However, such chemical processing can either destroy or adversely modify the physiologically active molecules. Before chemical processing, the part of the herbs is chosen from where the chemicals are extracted like leaves, roots, fruits, stems, twigs, barks and flowers. Normally, such parts are selected because of their richness in desired active ingredients. The resulted samples, e.g. oil, wax, juice, tincture, powder, infusion and decoction obtained after the extraction procedure are then converted into solutions, gels, ointments, lo



tions, pastes and creams (Thornfeldt, 2005). This review endeavours and emphasizes on various biological activities and the benefits exerted by the phytochemicals in the field of herbal cosmeceuticals along with their extraction procedure, regulations, safety and associated future perspectives. The common botanicals used in herbal cosmeceuticals for exhibiting cosmetic and pharmaceutical activities have been enlisted in Table 1.

2. Applications

2.1. Herbs for skin care

Skin is the most exposed part of the body. It easily comes in contact with the surrounding environment (sun-rays, dirt, pollution, contaminants) and causes rashes, pimples, acne, skin darkening, skin diseases, etc. So, to maintain the health and hygiene of the skin, herbal cosmeceuticals are applied which not only maintain the hygiene of the skin but also enhance the skin condition and rejuvenate the skin from the cellular and molecular levels. The various skin care cosmeceuticals used in day-to-day life are antioxidants, sunscreens, anti-inflammatory agents, de-pigmenting and skin renewal agents.

2.2. Antioxidants

Antioxidants are defined as substances that reduce the damage caused by the presence of oxygen in the form of free radicals. Unrestrained subjection to UV-radiation actuate oxidation which produces several adverse reactions like sunburns, photo-aging, etc. UV-radiation is divided into three categories according to the wavelength involving how you using UVA (320-400 nm); UVB (280-320 nm) and UVC (200-280 nm).

Among these, UVA and UVB have a detrimental impact on the human beings. The mechanism through which the radiation damages the skin lies on the fact that when the skin comes in contact with the UV-radiations, the photo-oxidative reactions initiate, which in turn produce reactive oxygen species (ROS), like peroxide (R-O-O-R), superoxide (O_2^{-}), hydroxyl radicals (OH.) and singlet oxygen (O=O). The ROS generated, then stimulates the fibroblast which increases the expression of MMP-1 (Matrix Metallo Proteinase-1) and causes collagen degradation and decreases collagen synthesis. All these results finally lead to photo-damage of the skin. The oxidative reactions also activate the protein kinase C enzymes which then combine with protein, lipids, DNA and form cyclobutane pyridine dimers. Such dimers destroy the DNA configuration and produce skin sunburns, edema, cell apoptosis, etc. Another angle that focuses on the destructive effect of the radiation is the development of the oxidative stress environment. Such stress develops a huge amount of ROS within the body and damages the skin in two ways:

(a) Increasing elastin mRNA levels in dermal fibroblast which provides a change in the mechanism of elastin production and (b) Modification of the tissue proteins into their respective carbonyl derivatives which accumu-

S.No.	Phytochemicals	Nano-deliverymethods	Application	References
-	Rice bran oil which contains tocopherols and gamma- oryzanol	Nanoemulsion	Moisturizers	Bernardi etal., 2011
2	Raspberry seed oil containing anthocyanin	Lipid nanocarriers	Sunscreen	Niculae etal., 2014
3	Lavender extracts containing polyphenols	Polymeric nanoparticles	Anti-aging	Pereira etal., 2015
4	Rosemary extracts which contains flavonoid compounds	SLN	Antioxidants	Lacatusu etal., 2010
5	Aloe vera extracts containing aloesin	Liposomes	Skin care	Takahashi etal., 2009
9	Safflower extracts containing safflower yellow	NLC	Haircare	Kumar et al.,2011
7	D-Limonene	Nanoemulsion	Skin care	Lu etal., 2014
8	Quercetin	NLCs	Skin care	Guo etal., 2012
6	Hinokitiol	Nanocapsules	Hair care	Hwang and Kim, 2008
10	Propolis and lycopene	Nanoemulsions	Skin care	Butnariu and Giuchici, 2011

Common botanicals used in herbal cosmeceuticals.

Table 1



lates in the papillary dermis and produces photodamage to the skin (Afaq and Mukhtar, 2006; Setyowati, 2017).

Some evidences accounting for antioxidant activity of botanicals are as follows.

1. Camellia sinensis L. (Green tea): Camellia sinensis L. belongs to the family Theaceae and order Ericales. They originate from South East Asia and China and are extensively grown in forest edges and gaps at high altitudes in well-drained soils. Camellia sinensis L contains four types of catechins (8.5-20.6%), namely (-)-epicatechin (EC), (-)-epicatechingallate (ECG), (-)-epigallocatechin and (-)-epigallocatechin-3-gallate (EGCG) (Fig. 1) (Musdja et al., 2018). The common backbone of all these catechins (polyphenols) is flavan-3-ol. Among the four polyphenols, the maximum contribution was attributed to EGCG which contained approximately 40% of total polyphenols. These polyphenols act as ROS scavengers. They decrease the amount of ROS, which in turn decreases the oxidative stress and reduces the DNA damage and hence prevents the skin from the oxidative damage. These catechins also form inactive complexes by chelating with free iron and copper ions which in turn cease ROS generation and provide a protective effect against oxidative damage as well as photo-damage (Afaq and Mukhtar, 2006).

2. Punica granatum L. (Pomegranate) (Fig. 2): Punica granatum L. belongs to the family Lythraceae and order Myrtales. They originate from Iran and Northern India. Pomegranates are best grown in areas with warm and low-humidity and prefer soil with neutral pH. The active components of pomegranate are phenolic compounds, anthocyanidins viz. delphinidin, cyaniding and pelargonidin and hydrolyzable tannins like punicalin, pedunculagin, punicalagin, gallagic as well as ellagic acids. About 50% of the total fruit weight corresponds to the peel which comprises of bioactive components (Mphahlele et al., 2016). They also act as ROS scavengers. Apart from it, they have a ferrous chelating activity which decreases the availability of free iron and reduces the chances of catalyzing ROS. In pomegranate, punicalagin shows the highest ferrous chelating activity, as well (Afaq and Mukhtar, 2006; Aloqbi et al., 2016).

3. Uncaria gambir Roxb. (Gambir) (Fig. 2): Uncaria gambir Roxb. belongs to the family of Rubiaceae and order Gentianales. They are well-distributed throughout tropical regions, like Southeast Asia, Africa and Southeast America. The chemical composition of Gambir includes catechin, catechu acid and quercetin. Catechin (40-80%) shows potent antioxidant activity (Aloqbi et al., 2016). Gambir also contains various derivatives of catechin like EC, ECG and EGCG, etc. They inactivate the ROS generation which in turn protects the DNA damage and hence prevents skin damage (Kidd, 2009).

4. Mushroom (Fig. 2): Mushroom is the spore-bearing fruiting body of a fungus which grows above ground or soil. It belongs to the Fungi kingdom and Basidiomycota divisions. Mushroom needs a moist and shady place to grow and exhibits its relevant antioxidant property by scavenging ROS and suppressing MMP-1 expression. In addition, the mushroom has reducing power that exhibits ferric reducing antioxidant properties (FRAP). Various species of mushrooms that show antioxidant properties are *Agaricus sp* (phenolic compounds, β -carotene, catechin, gallic acid, etc.); *Clavaria sp*; *Auricularia sp*; *Lycoperdon sp*; *Lactarius sp*; *Hypholoma sp*, etc. They also contain some flavonoid and phenolic compounds (Taofiq et al., 2016).

5. Allium sativum L. (Garlic) (Fig. 2): Allium sativum L belongs to the family of Liliaceae and order Liliales. They are native to Central Asia and North-eastern Iran and are grown in warm and moderate climatic conditions. The antioxidant activities are shown by alliin (0.6-1.4%, fresh weight) (Wikandari et al., 2020), vitamin C and flavonoids. They scavenge ROS and provide a protective effect against oxidative damage (Bhandari et al., 2014). 6. Zingiber officinale Roscoe (Ginger) (Fig. 2): Zingiber officinale Roscoe belongs to the family Zingiberaceae and order Zingiberales. They are distributed in South and Southeast Asia, Africa, Latin America, the Caribbean and Australia and are well-grown in hot and humid conditions with loamy soils. The phytochemicals responsible for antioxidant activity are gallic acids, 6-shogaol (2.76 mg/g), 6-gingerol (1.42 mg/g) oleoresin and polyphenols (Teng et al., 2019). They reduce the excessive oxygen via ferric-reducing antioxidant properties (FRAP) (Mao et al., 2019).

7. Ocimum basillicum L. (Basil) (Fig. 2): Ocimum basillicum L belongs to the family of Lamiaceae and order Lamiales. They are native to tropical Asia, Africa, America and Europe and are well-grown in warm temperate zone with annual daytime temperatures ranges from 18 to 27 °C and annual rainfall ranges from 1000 to 1600 mm. Basil is intolerant to frosts. Rosmarinic (10 mg/g dry weight) (Kintzios et al., 2003) and caffeic acid are the phytochemicals that show antioxidant activity. They also act as ROS scavengers (Marwat et al., 2011).

8. *Curcuma longa* Linn. (Turmeric) (Fig. 2): *Curcuma longa* Linn. belongs to the family of Zingiberaceae and order Zingiberales. They originate from South and Southeast Asia, Vietnam, China and Western India and are grown in humid and warm weather with a lot of rainfall. Curcuminoids (96.5%) (Pushpakumari et al., 2015) are the phytochemicals that show ROS scavenging activity and act as an antioxidant (Sabale et al., 2013).

9. *Crocus sativus* L. (Saffron) (Fig. 2): *Crocus sativus* L. belongs to the family of Iridaceae and order Liliaceae. They originate from European countries, Western Asia, Northern India and China and are grown best in cool winters to hot summer with heavy rainfall. The phytochemicals responsible for exhibiting antioxidant activity are safranal (2.5%) (Rezaee and Hosseinzadeh, 2013) and crocin. They show ABTS and DPPH radical scavenging activities (Rahaiee et al., 2015).

2.3. Sunscreens

Sunscreens are the first-line defense against UV-radiations. They protect photo-damage through two mechanisms- (a) UV-absorption and (b) UV-reflection. UV absorption deals with the absorption of the radiations and converting them into heat. In this way, they decrease



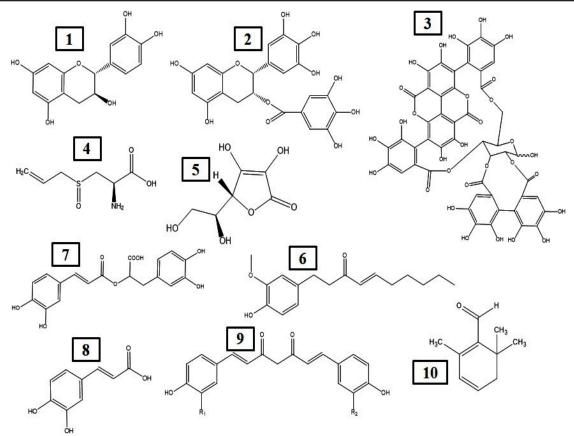


Fig. 1. Structures of phytochemicals showing antioxidants property: 1. Catechin, 2. Epigallocatechin-3-gallate (EGCG), 3. Punicalagin, 4. Alliin, 5. Vitamin C, 6. 6-Shagaol, 7. Rosmarinic acid, 8. Caffeic acid, 9. Curcuminoids, 10. Safranal.

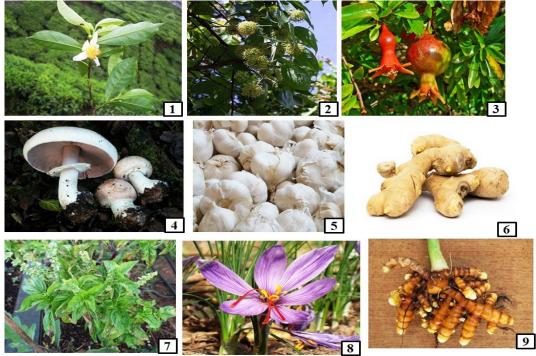


Fig. 2. Botanicals showing antioxidant activity: 1. *Camellia sinensis* L., 2. *Uncaria gambir* Roxb., 3. *Punica granatum* L., 4. *Agaricus* sp., 5. *Allium sativum* L., 6. *Zingiber officinale* Roscoe., 7. *Ocimum basillicum* L., 8. *Crocus sativus* L., 9. *Curcuma longa* Linn.



the harmful effect of UV-radiation. On the other hand, UV-reflection deals with the scattering of the radiations. Herbal sunscreens act by both mechanisms. In fact, they absorb the erythemal portion of radiation and effectively scatter the remaining portion of the radiations. It should be noted that a good sunscreen must possess certain ideal characteristics to perform effectively: (a) Absorption of radiation preferentially over the wavelength range of 280-320 nm, (b) Being neutral, stable in the presence of light, heat and perspiration and (c) Easily soluble in suitable vehicles. One important term associated with sunscreen is sun protection factor (SPF) which is the number that defines how much protection a sunscreen should provide when applied to a skin with a thickness of 2 mg/cm² (Afaq and Mukhtar, 2006; Camouse et al., 2009).

Some examples of botanicals showing sunscreen activity are given below:

1. Uncaria gambir Roxb (Gambir): The photo-protective activity towards UV-A and UV-B is performed by catechin. It is preferred over chemical sunscreens because catechins provide broad-spectrum UV absorption as well as protection against oxidative stress. It was reported that many other flavonoids like quercetin and luteolin also act as good UV blockers (Setyowati, 2017). 2. Camellia sinensis L. (green tea and white tea): Camellia sinensis L contains polyphenols that scatter the UV-radiations and thus, have a photo-protective effect. They also show partial prevention of DNA damage by blocking UV-induced oxidation. However, white tea is the least processed and hence contains excessive levels of polyphenols but at present there are not enough published data to encounter its usage against the detrimental effect of UV-radiation (Camouse et al., 2009).

3. Aloe barbadensis Miller (Aloe Vera): Aloe barbadensis Miller belongs to the family of Liliaceae and order Asparagales. They originate from the South-West Arabian Peninsula and are also found in North Africa, Sudan, Canary Islands, Cape Verde and Madeira islands. *Aloe barbadensis* Miller grows well in tropical and subtropical territories, in arid sandy conditions that contain clay and lime. The aloe gel encompasses a non-starch polysaccharide, named acemannan (Fig. 3) which reduces skin damage when exposed to radiation. Acemannan (non-starch polysaccharide) represents 62.3% and 57.6% of the dry weight of the rind and pulp, respectively (Hui, 2013). Aloe gel scavenges hydroxyl radicals and prevents the suppression of superoxide dismutase and glutathione peroxidase (Devi and Y, 2005).

4. *Phyllanthus emblica* L. (Amla/Indian gooseberry) (Fig. 4): *Phyllanthus emblica* L belongs to the family Euphorbiaceae and order Euphorbiales. They are distributed around Indo Malesia belt, SriLanka, South China along with India and are grown in grassy areas and village groves with 12-13 hrs daylength. The UV-protectant activity is shown due to the antioxidant properties of phyllembin (18-35%) (Jansen and Cardon, 2005), flavonoids and kaempferol. They are capable of scavenging ROS species (Kulkarni and Kendre, 2014).

5. Solanum lycopersicum L. (Tomato): Solanum lycopersicum L belongs to the family Solanaceae and order

Solanales. They are native to Western South America, central Ecuador, through Peru, Northern Chile and Galápagos Islands and require temperate climates for their growth. Lycopene (35-96%) (Rath et al., 2009) is the active phytochemical that scavenges hydroxyl radical and provides a protection against harmful effects of UV-radiation thereby delivering a sunscreen activity (Mishra et al., 2011).

6. *Terminalia chebula* Retz (Gall nut): *Terminalia chebula* Retz belongs to the family Combretaceae and order Myrtales. They are widely distributed in South and Southeast Asia and are grown in dry slopes. The aqueous extracts of phytochemicals show DPPH radical scavenging activity and therefore provide a UV-protectant activity (Bag et al., 2013).

7. Daucus carota L. (carrot): Daucus carota L belongs to the family Apiaceae and order Apiales. They are native to Afghanistan, Himalayan mountains and adjacent regions of Russia, Iran, India, Pakistan and Anatolia and are grown in rough grassland, weedy meadows, prairies and wasteland. β -Carotene (21%) is the active phytochemical that absorbs both UV-A and B spectra and protects the skin from harmful UV radiation (Pritwani and Mathur, 2017).

8. Juglans regia L. (Walnut): Juglans regia L. belongs to the family Juglandaceae and order Juglandales. They are native to central Asia and Europe and require long warm season for growth. Juglone (0.5 g/100 g dry weight) (Thakur, 2011) is the active phytochemical that reacts with keratin and forms sclerojuglonic showing UV protection activity. The other phytoconstituents responsible for showing UV-protectant activity are aqueous extracts of polyunsaturated fatty acids, linolenic acid, linoleic acid and glyceryl triacylates (Anitha, 2012).

2.4. Anti-inflammatory

Inflammation is a physiological condition where swelling occurs either due to microbial infestation or by the release of certain inflammatory mediators. It is considered as one of the defense mechanisms of the body. When the body gets injured or invaded by the microorganisms, the damaged cells releases some chemicals called inflammation mediators. These mediators cause leakage of the blood vessels, which get accumulated into the tissues and cause swelling which further prevents the invasion. If these inflammatory mediators are released in high amounts, the immune cells get overexpressed and cause diseases like Inflammatory Bowel Diseases (IBN), etc. The inflammatory mediators involve interleukins (IL, IL-6, IL-8), tumor necrosis factor (TNF-α), nuclear factor-kß (NF-kß), intercellular adhesion molecules-I, COX-2, 5-LOX, PGE, and inducible nitric oxide synthase (iNOS) (Kidd, 2009; Taofiq et al., 2016).

Some botanicals showing anti-inflammatory activity are listed below:

1. *Aloe barbadensis* Miller. (Aloe Vera): The aloe vera gel contains two maloyl glucans (Fig. 5), named veracylglucan B and veracylglucan C which show significant anti-inflammatory activities (Periasamy et al., 2014). Maloyl glucans were the soluble sugars and it was reported



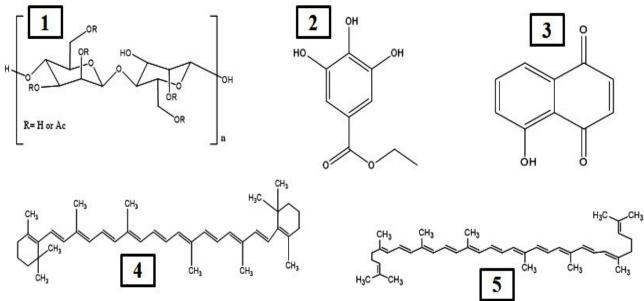


Fig. 3. Structures of phytochemicals showing UV-protection property: 1. Acemannan, 2. Phyllembin, 3. Juglone, 4. β -Carotene, 5. Lycopene.

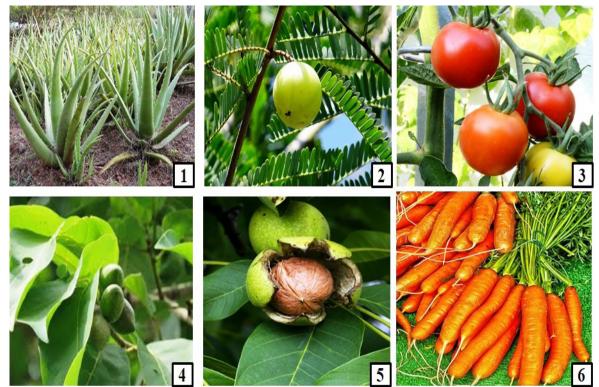


Fig. 4. Botanicals showing sunscreen activity: 1. *Aloe barbadensis* Miller., 2. *Phyllanthus emblica* L., 3. *Solanum lycopersicum* L., 4. *Terminalia chebula*, 5. *Juglans regia*, 6. *Daucus carota*.



that the percentage of soluble sugars in aloe vera gel was found to be 11.2% and 16.5% of the dry weight of the rind and pulp, respectively (Hui, 2013). Apart from these, anti-inflammatory activity is also shown by phytochemicals like lupeol, campestrol, β -sitosterol and C-glucosylchromone. They show anti-inflammatory activity by inhibiting the COX pathway and reducing prostaglandin E2 produced from the arachidonic acid (Devi and Y, 2005).

2. Mushroom: The various species of mushrooms that show anti-inflammatory action are *Agaricus sp*, *Bisporus sp*, *Phelllinus sp*, *Cordyups sp*, *Antrodia sp*, *Pleurotus sp*, etc. The active components responsible for showing anti-inflammatory efficacy are terpenes, phenolic compounds, polysaccharide-protein complex, etc. They reduce the levels of inflammatory mediators like interleukins, TNF- α and PGE2 (Taofiq et al., 2016).

3. Silybum marianum L. (Milk thistle) (Fig. 6): Silybum marianum L. Gaertn. belongs to the family of Asteraceae and order Asterales. They are found in the Mediterranean region, Asia and Northern Europe but they have now spread to temperate regions of the world and are well-grown in sub-humid, warm-temperate regions occurring on fertile, alluvial or volcanic soils. The active ingredient of *Silybum marianum* L. Gaertn extract is a flavonolignan, named silybin. About 50-70% of the extract was comprised of silybin (Bijak, 2017). It acts as a potent inhibitor of nuclear factor- $k\beta$ which decreases cell differentiation and stress response and thus provides an efficient anti-inflammatory activity (Kidd, 2009).

4. *Curcuma longa* L. (Turmeric): The anti-inflammatory activity is shown by curcumin which contains 50-60% of curcuminoids (Chakraborty et al., 2018). Curcumin down regulates NF-k β , LOX, iNOS, COX-2 and antagonizes activator protein 1 (AP-1), thus regulates cellular differentiation and proliferation. Taking into account these behaviors, *Curcuma longa* L. provides an enhanced anti-inflammatory activity (Kidd, 2009).

5. Syzygium aromaticum L. (Clove): Syzygium aromaticum L belongs to the family Myrtaceae and order Myrtales. They are distributed in Moluccas, Mauritius, Madagascar, India, Sri Lanka, Zanzibar, Brazil, the West Indies and Pemba and are grown in maritime forests, well-drained sandy area with acidic loamy soil. Eugenol (16.0%) (Narayanan and Natu, 1974) exhibits reduction of cytokines and inhibition of COX levels and as a result provides an effective anti-inflammatory activity (Azab et al., 2016).

6. Allium cepa L. (Onion): Allium cepa L. belongs to family Liliaceae and order Liliales. They originate from Central Asia and are grown in temperate regions. The anti-inflammatory activity of Allium cepa L. is shown by quercetin (77-93%) (Kwak et al., 2017) that reduces cytokines and inhibits COX, LOX and NFkB (Azab et al., 2016).

7. Allium sativum L. (Garlic): The anti-inflammatory activity is shown by allicin (2.5-4.5 mg/g of fresh weight) (Wikandari et al., 2020). It reduces the level of PGs, NO, IL-1 β , IL6 and TNF- α and increases the levels of IL-10 levels (Bose and Laha, 2013).

8. Solanum lycopersicum L. (Tomato): The presence of

ferulic acid (0.29-6 mg/0.1 kg) (Kumar and Pruthi, 2014) in tomato is responsible for exerting anti-inflammatory activity. Ferulic acid reduces cytokines and inhibits the action of COX-2, iNOS, NFkB, which in turn delivers an efficient anti-inflammatory property (Azab et al., 2016). 9. *Hibiscus tiliaceus* L. (Coast cottonwood): *Hibiscus tiliaceus* L. belongs to the family Malvaceae and order Malvales. They are well-distributed in coastal areas of Africa, America, Asia, Australia and the Pacific Islands and are grown around beaches, rivers and mangrove swamps having 900-2,500 mm of annual rainfall. The anti-inflammatory activity is shown by 3-hydroxyanthranilic acid. It reduces the level of cytokines, LTs, PGs and NO levels and inhibits the activity of COX, iNOS, 5-LOX and NFkB (Azab et al., 2016).

2.5. De-pigmenting agent

Skin lightening and anti-hyper pigmenting agents are known as de-pigmenting agents. The skin darkening is due to the presence of melanin in the body. When the skin comes in contact with UV-radiation, the keratinocytes are stimulated and secret α -MSH (α -melanocyte stimulating hormone). The α -MSH then binds with melanocortins I receptor present on the surface of melanocyte and produces melanin. This process of melanin formation is called melanogenesis. The process of melanogenesis is controlled by modulating various factors taking part in the process like the up-regulation of MITF (Melanocyte Inducing Transcription Factor) and down regulation of tyrosinase activity and ERK (extracellular signal-regulated kinases) signaling pathway. Hydroguinone was considered as one of the best de-pigmenting agents but due to certain adverse effect, it is being banned in most of the countries (Kanlayavattanakul and Lourith, 2018).

Some examples of botanicals showing de-pigmenting activity are discussed as follows.

1. Citrus limon L. (lemon) and Citrus sinensis L. (sweet orange): Citrus limon L. and Citrus sinensis L. belong to the family of Rutaceae and order Rutales. Citrus fruits are grown in South East Asia, particularly, Indo-Malaysia, China, New Guinea and central Australia to New Caledonia. The *Citrus* fruits are found in tropical as well as sub-tropical regions where the temperature ranges from 16 °C to 29 °C. They are also sensitive to cold temperatures and heavy rains. The de-pigmenting activity is observed by hesperidin (Fig. 7). The amount of hesperidin in Citrus fruits was found to be 28.6 mg/100 mL (Gattuso et al., 2007). They show de-pigmenting activity by inhibiting tyrosinase activity, which further decreases the release of melanin. In addition, they protect the skin from UV-radiation induced oxidative damage of collagen and fibroblast. Hence, hesperidin acts as a prospective skin lightening agent (Kanlayavattanakul and Lourith, 2018).

2. *Glycyrrhiza glabra* L. (Licorice) (Fig. 8): *Glycyrrhiza glabra* L. belongs to the family Fabaceae and order Fabales. They are native to the Mediterranean region and some parts of Asia and are well-grown in fertile, sandy, or clay soil near a river or stream, or wherever, water is avail-



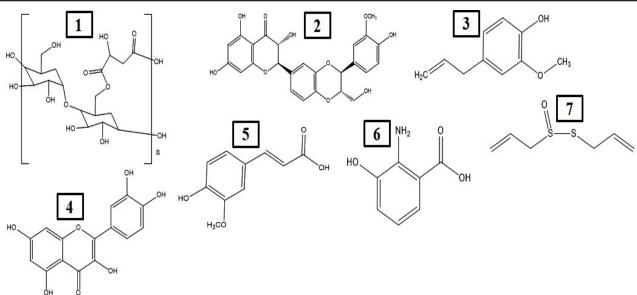


Fig. 5. Structures of phytochemicals showing anti-inflammatory property: 1. Maloyl glycan, 2. Silybin, 3. Eugenol, 4. Quercetin, 5. Ferulic acid, 6. 3-Hydroxyanthranilic acid, 7. Allicin.

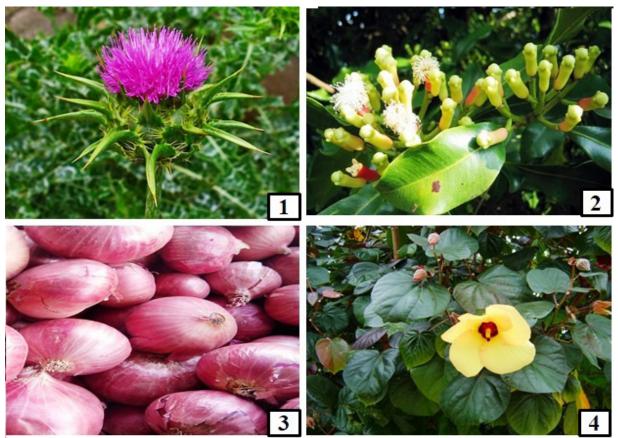


Fig. 6. Botanicals showing anti-inflammatory activity: 1. *Silybum marianum* L., 2. *Syzygium aromaticum* L., 3. *Allium cepa* L, 4. *Hibiscus tiliaceus* L.

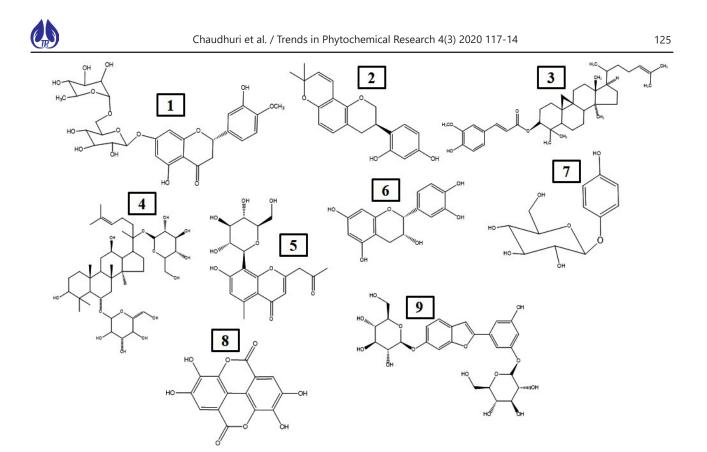


Fig. 7. Structures of phytochemicals showing de-pigmenting property: 1. Hesperidin, 2. Glabridin, 3. gamma-Oryzanol, 4. Ginsenoside, 5. ALoesin, 6. Procyanidin, 7. Arbutin, 8. Ellagic acid, 9. Mulberroside F.

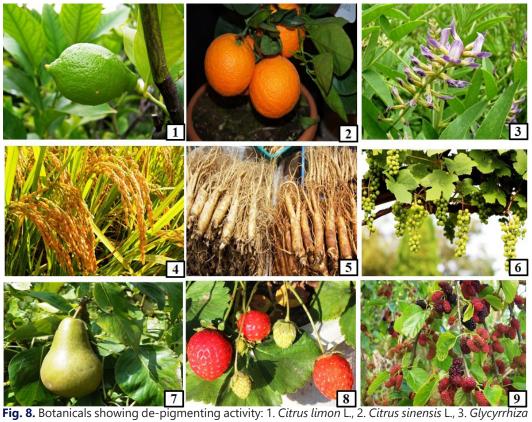


Fig. 8. Botanicals showing de-pigmenting activity: 1. *Citrus limon* L., 2. *Citrus sinensis* L., 3. *Glycyrrhiza* glabra L., 4. *Oryza sativa* L., 5. *Panax ginseng*, 6. *Vitis vinifera* L., 7. *Pyrus communis* L., 8. *Fragaria* ananassa Duchesne., 9. *Morus alba* L.



able, or under cultivation where it can be irrigated. The extract contains an ingredient, named glabridin which inhibits tyrosinase activity and contains approximately 20% glabridin (Ao, 2010). Other components that show the de-pigmenting activity of *Glycyrrhiza glabra* L. are glabrene, licuraside, isoliquiritin, licocholcone A, etc. (Zhu and Gao, 2008; Kanlayavattanakul and Lourith, 2018).

3. Oryzasativa L. (Rice): Oryzasativa L. belongs to the family Poaceae and order Cyperales. Rice is well cultivated in Japan, Brazil, China, India, Indonesia, Bangladesh, Vietnam, Thailand, Myanmar and the Philippines. They are well-grown in hot and humid climate where the average temperature ranges from 21 to 37 °C. Oryza sativa L. contains gamma-oryzanol as a key ingredient of rice bran oil. Gamma-oryzanol is a mixture of ferulic acid esters of sterol and triterpene alcohols comprising approximately 1-2% of total extract (Patel, 2004). The above phytochemicals exert their activity as a de-pigmenting agent by inhibitin cellular melanin formation. Rice extract contains resveratrol that also shows de-pigmenting activity through tyrosinase inhibition. Thus, Oryza sativa L. functions as an efficient skin lightening agent (Kanlayavattanakul and Lourith, 2018). 4. Panax ginseng (Asiatic ginseng): They belong to the family Araliaceae and order Araliales and originate from mountainous regions of Russian, North-eastern China and the Korean Peninsula and are well-grown in a cool climate with a temperate climate, broad-leaved forests and annual rainfall of between 50 and 100 cm. The de-pigmenting activity is shown by ginsenosides. It was observed that the ginseng root contained only 2-3% ginsenoside (Khan et al., 2015). Ginsenoside shows activity against α -MSH generation and inhibits the secretion of α -MSH and as a result decreases the production of the melanin (Zhu and Gao, 2008).

5. *Aloe barbadensis* Miller. (Aloe Vera): Aloesin (10-30%) (Fouillaud et al., 2018) present in A. *barbadensis* Miller decreases tyrosinase activity and DOPA oxidase and provides a de-pigmenting activity (Choi et al., 2002).

6. *Vitis vinifera* L. (Grapevine): *Vitis vinifera* L. belongs to the family Vitaceae and order Rhamnales. They are distributed along the Mediterranean basin and are found in humid forests and streamside. Procyanidins (92-95%) (Union, 2012) are the active phytochemicals that decrease the activity of tyrosinase and increase the ROS scavenging activity (Zhu and Gao, 2008).

7. *Pyrus communis* L. (European Pear): *Pyrus communis* L. belongs to the family Rosaceae and order Rosales. They are native to China, Asia and regions of the Middle East and are well-grown in temperate regions. Arbutin (8.13%) (Bulduk and Sahin, 2016) shows skin de-pigmenting activity. It decreases the activity of tyrosinase and DHICA polymerase (Zhu and Gao, 2008).

8. Fragaria ananassa Duchesn (Strawberry): Fragaria ananassa belongs to the family Rosaceae and order Rosales. They originate from Europe, East and Southeast Asia, North America and some parts of South America and are well-grown in semi-shade area with moist soil. Ellagic acid (0.63 mg/g of dry weight) (Muthukumaran et al., 2017) decreases MC proliferation and inhibits tyrosinase activity and hence provides an efficient skin de-pigmenting activity (Shimogaki et al., 2000).

9. Morus alba L. (Mora): Morus alba belongs to the family Moraceae and order Urticales. They are distributed along central and Eastern China and prefer a warm, moist area with well-drained loamy soil for their growth. The de-pigmenting activity is shown by mulberroside F which decreases tyrosinase activity and increases ROS scavenging activity (Lee et al., 2002).

2.6. Skin renewal agents

Skin renewal agents are the substances that treat and prevent acne and wrinkles, moisturize the skin, prevent the aging of skin, etc. Acne is a skin disease by which the skin gets inflamed and causes spots and pimples. It could be explained by emphasizing on the fact that our skin contains numerous hair follicles or pores which contain sebaceous glands that secrete sebum. When the amount of sebum gets increased, the pores or hair follicles get clogged. This provides a chance to the bacteria, named Propionibacterium acnes to get trapped within such pores and multiply. The multiplication then causes redness as well as swelling, which is termed as acne. Wrinkles similar to acne, is a skin condition where the skin develops ridges, creases or folds. The connective tissues of the skin contain numerous specialized cells called fibroblasts which produce two types of proteins, collagen and elastin. Collagen provides firmness and elastin provides stretches to the skin. Wrinkle develops when any damage occurs to these proteins. Skin aging is also a skin-oriented disruption caused by intrinsic and extrinsic factors. Intrinsic aging involves chronological aging, i.e. aging with time and extrinsic aging involves stimulation by external stimuli like UV-radiations, pollution, smoking, stress, sleep deprivation and utmost temperature. Out of these external factors, UV-radiation plays a significant role in skin aging. The UV-radiation stimulates matrix metalloproteinase (MMP) upon exposure which causes the breakdown of collagen and thereby develops aging. UV-radiation also produces ROS which indirectly accelerates skin aging. Dry skin can also lead to skin aging. The skin gets dried up due to many reasons like dry weather, dehydration, using harsh bar soaps, not consuming the right foods, itching, scratching, etc. So, it is necessary to consume and apply certain botanicals in forms of foods and cosmeceuticals respectively to make the skin hydrated and moist (Sumit et al., 2012; Campa, 2018).

Some botanicals showing skin renewal activity have been enlisted below:

1. Aloe barbadensis Miller. (Aloe vera): Aloe barbadensis Miller contains numerous ingredients that modulate the skin condition. Aloe vera contains mucopolysaccharides that bind the moisture within the skin, amino acids that soften the skin and zinc that act as astringent, thus tightening the pores and restricting the release of water from the skin. The presence of acemannan in Aloe vera also helps in stimulating the fibroblast, as a result more collagen and elastin get secreted which enhances the flexibility of the skin (Cho et al., 2009; Kanlayavattanakul



and Lourith, 2018).

2. Daucus carota L. (carrot): Carrots are rich in α - and β -carotene. The amount of carotenes in carrot ranges from 60 to120 mg/100 g (Fikselova et al., 2008). The carotenes act as a skin rejuvenator and anti-wrinkle agent. They produce new cells, develop the growth of tissue and thus reduce the formation of wrinkles and promote the renewal of tissue and cells (Sumit et al., 2012).

3. Cocos nucifera L. (Coconut): It belongs to the family of Arecaceae and order Arecales. Coconut is native to coastal areas of South-East Asia mainly Malaysia, Indonesia, Philippines and Papua New Guinea. They are also cultivated across Africa, America and Australia. Coconut is well habitat on sandy beaches and coastal areas in tropical and sub-tropical areas of the world with regular rainfall ranges from 1500 mm to 2500 mm annually and high temperature ranges from 21 to 30 °C. The oil of the coconut is used as cosmeceuticals and contains about 90-95% saturated triglycerides (Fig. 9) which act as emollient and hence moisturize the dry or dehydrated skin (Krishna et al., 2010). Inside the body, the triglycerides are broken down into glycerine and fatty acids via lipases. Glycerine acts as a potent humectant that absorbs the moisture from the environment and hydrates the skin (Campa and Baron, 2018).

4. Ocimum basilicum L. (Basil): It belongs to the family Lamiaceae and the order Lamiales. Basil is widely distributed across Tropical Asia which includes China, India, Myanmar, Thailand, Cambodia, Laos, Vietnam, Malaysia, Indonesia, Philippines and New Guinea. It is widely used as an anti-acne and the active phytochemicals responsible for this activity are linalool and estragole. The amount of estragole and linalool in basil ranges from 22 to 38% and 21 to 37%, respectively (Da Costa et al., 2015). Apart from these, other ingredients like o-cymene, citral, α -pinene and camphene also play an important role in skin renewal. They inhibit both COX and LOX pathways and prevent inflammation which provides an anti-acne activity (Campa and Baron, 2018). 5. Coffea arabica L. (Arabica coffee) (Fig. 10): Coffea arabica L. belongs to the family Rubiaceae and order Gentianales. They are native to Northeast tropical Africa and are best grown in regions with cool and humid climate. Chlorogenic acids (3.5-7.5% dry weight) (Jeszka-Skowron et al., 2016), caffeine and melanoidins are the phytochemicals that prevent aging of the skin through the anti-inflammatory activity (Del Castillo et al., 2016).

6. *Panax ginseng* (Asiatic ginseng): Ginsenosides (2-3%) (Khan et al., 2015) induces synthesis of type I collagen and thus tightens the skin and exhibits skin-rejuvenation activity (Lee et al., 2007).

7. Rosmarinus officinalis L. (Rosemary): Rosmarinus officinalis L. belongs to the family Lamiaceae and order Lamiales. They originate from Mediterranean region and are grown in low bush with limestone-rich soil. The skin renewal activity is shown by the presence of rosmarinic acid (approx. 58.5 mg/g of dry weight) (Shekarchi et al., 2012) which exhibits anti-inflammatory and antioxidant activities (Del Baño et al., 2003). 8. *Phoenix dactylifera* L. (Date-palm): *Phoenix dactylifera* L. belongs to the family Arecaceae and order Arecales. They are native to the tropical or subtropical regions of Southern Asia or Africa and require sandy or saline soils with hot and dry climate for their growth. Phenolic acids, vitamins and ascorbic acid promote synthesis of collagen and improve skin hydration level (Meer et al., 2017).

9. Humulus lupulus L. (Hops): Humulus lupulus L. belongs to family Cannabaceae and order Urticales. They are native to Europe, Western Asia and the USA and are well-grown in hedgerows, woodlands and sunny wastelands. Xanthohumol (0.2-1.0%), humulones and lupulones are the active phytochemicals responsible for skin renewal activity and show oxygen radical absorbance activity (Sahatpure and Hills, 2018).

2.7. Herbs for hair care

Hair care denotes the health and hygiene of the hair. Hair is another important part of the body that is highly exposed to the external environment and experiences extensive damages like alopecia (hair loss), dandruff, etc. So, to provide better hair conditions, hair care cosmeceuticals are used.

To give a deeper insight into this topic, some relevant herbal cosmeceuticals for hair care are argued as follows.

2.7. 1. Anti-dandruff

Dandruff is a condition that affects the scalp by causing flakes, accompanied by itching. It occurs for many reasons, like extensive oil secretion from the sebaceous gland, release of metabolic by-products of microorganisms like *Malassezia sp.* (fungus) and some allergic reactions. It is observed that dandruff widely occurs due to the presence of a microorganism, named *Malassezia* sp. formerly, named as *Pityrosporum ovale*. This fungus gets activated on weather change, hormonal disturbances together with stress and releases oleic acid by hydrolysis of sebum in the presence of enzyme lipase. The oleic acid released helps the fungus to proliferate further and to penetrate the top layer of the skin which is observed in the form of flakes (Potlur et al., 2013; Prashant et al., 2017).

Some relevant data in literature relating to botanicals showing anti-dandruff activity are given below:

1. *Lawsonia inermis* L. (Henna): *Lawsonia inermis* L belongs to the family of Lythraceae and the order of Myrtales. The henna is native to Northern Africa, Western and Southern Asia and Northern Australia. They are well-grown in dry and semi-arid areas. For anti-dandruff purposes, henna leaves are used in dried powdered form. They contain a dye molecule, named lawsone (Fig. 11). A dried, powdered leaf of henna contains 0.5 to 1.5 percent lawsone (Prakash and Majeed, 2015). Lawsone has a natural affinity with the proteins present within the hair. As a result, it binds with the protein and provides stains onto the hair shaft and prevents the activity of lipase. As a result, the hydrolysis of oleic acid is



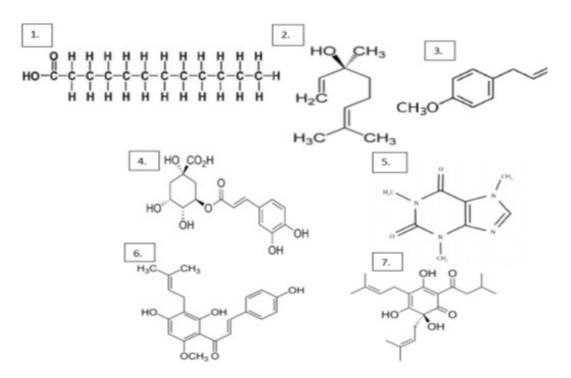


Fig. 9. Structure of phytochemicals showing skin-renewal activity: 1. Saturated triglycerides, 2. Linalool, 3. Estragole, 4. Chlorogenic acids, 5. Caffeine, 6. Xanthohumol, 7. Humulones.



Fig. 10. Botanicals showing skin renewal activity: 1. Cocos nucifera L., 2. Coffea arabica L., 3. Rosmarinus officinalis L., 4. Phoenix dactylifera L., 5. Humulus lupulus L.



prevented and provides an anti-dandruff activity (Potluri et al., 2013).

2. *Melaleuca alternifolia* (Tea Tree) (Fig. 12): It belongs to the family of Myrtaceae and order Myrtales. Tea tree is native to Australia and grows along streams and swampy places. The oil obtained from the leaves of the tea tree is used as an anti-dandruff agent. The active phytochemical of tea tree is terpinen-4-ol which comprises 40.4% of total components. The other components of tea tree such as α -terpineol, linalool, α -pinene and β -pinene also show antidandruff activity (Noumi et al., 2011). These components penetrate the cell membrane of the fungi, disrupt the permeability and membrane fluidity, prevent fungal growth which finally reduce the irritation and promote a healthier scalp (Hammer et al., 2004).

3. *Citrus limon* L. (lemon): The lemon juice or lemon pulp is used for exerting an anti-dandruff activity. They contain high amounts of ascorbic acid (vitamin C) that restores the pH of the scalp. The amount of ascorbic acid in lemon was found to be 57.5 mg/100 g (Adewole and Talabi, 2015). The undisturbed pH of the scalp provides an unsuitable environment to the fungi, which further inhibits their proliferation and growth (Potluri et al., 2013; Prashant et al., 2017).

4. *Sapindus mukorossi* Gaertn. (Reetha): It belongs to the family Sapindaceae and the order Sapindales. Reetha is distributed to some regions of Asia, Australia, North America and South America. They are well-grown in temperate to tropical regions of North India and Nepal in the presence of deep clayey loam soil with an annual rainfall of 150 to 200 cm. Reetha oil obtained from the seed coat is used for exhibiting anti-dandruff activity (Dsvgk et al., 2013). Saponins are the active phytochemicals present in the fruit. The average amount of saponin ranges from 10% to 11.5% (Upadhyay and Singh, 2012). Saponins act as cleansers which prevent the accumulation of oil on the scalp and hence inhibit the action of the fungi on the scalp (Prashant et al., 2017).

5. Acacia concinna Linn (Shikakai): Acacia concinna Linn. belongs to the family Fabaceae and the order Fabales. It is native to Asia, Southern China, Malaysia and parts of central and South India and is widely grown in warm plains. Shikakai oils obtained from pods are used as a hair cleanser. The hair cleanser activity is exhibited by saponins present in the highest amount within the pods (20.8%) (Poomanee et al., 2017). Saponins remove the oil and dirt from the hair and act as a natural hair conditioner. They also help in maintaining the pH of the scalp. Other phytochemicals of shikakai that show hair cleansing activity are lupeol, spinasterol, spinasterone, lupenone, betulin, betulinic acid, betulonic acid, etc. (Pal et al., 2018).

2.7.2. Alopecia

Alopecia means loss of hair from some or all areas of the body usually from the scalp. There are two types of alopecia, namely Alopecia areata and Androgenetic alopecia. Androgenetic alopecia occurs in both the genders and is characterized by a particular pattern of hair loss. Alopecia areata is an autoimmune disorder that results in the loss of hair from the scalp and other parts of the body. The various causes of alopecia are nutritional deficiencies, DHT and 5α -reductase activity as well as reduction of blood circulation to the scalp (Kaushik et al., 2011).

In this relation, the most important botanicals used for the treatment of alopecia are as follows.

1. Lavandula angustifolia: Lavandula angustifolia belongs to the family Lamiaceae and the order Lamiales. They are native to the Canary Islands to India through the Mediterranean region and are typically grown in arid and stony terrain with soil of neutral pH. The oil obtained from the flowering tops of Lavandula angustifolia is used for exhibiting anti-alopecia activity. Triterpenoids are the active phytochemicals exerting anti-alopecia activity which is approximately 0.12 g/100 g dry weight (Jager et al., 2009). Lavandula angustifolia is used in aromatherapy. The essential oils enter the body either through the nasal (inhalation) or through the skin and stimulate the hair follicles which increase the blood circulation in the scalp and subsequently enhance the hair growth (Kaushik et al., 2011).

2. Allium cepa L .: The oil obtained from the cloves of Allium cepa L. is used for its anti-alopecia activity. Sulphur containing compounds like allicin are the active phytochemicals exerting anti-alopecia activity. Allicin represents 70% of the overall thiosulfinates present in the cloves (Rahman, 2007). They are also used in aromatherapy. The oil increases the blood circulation in the scalp and stimulates hair regrowth (Kaushiketal., 2011). 3. Bacopa monnieri L.: Bacopa monnieri L belongs to the family Scrophulariaceae and the order Scrophulariales. They originate from tropical Asia across Asia, Africa, the Arabian Peninsula, Australia, America and the Caribbean and are well-grown in terrestrial and submerged aquatic conditions. The oil obtained from the entire plant is used for exhibiting anti-alopecia activity. Bacosides (Fig. 13) and triterpenoids saponins are the phytochemicals responsible for anti-alopecia activity. Bacoside comprises 55% of the extract by weight (Patel, 2020). It enhances hair growth by providing nutritional support and elevates the level of the minerals comprising vitamin A, vitamin B, vitamin C, vitamin D, vitamin E, iron, selenium and zinc required for hair growth. Also, it acts as the nerve stimulant (Kaushik et al., 2011).

4. *Panax ginseng:* The oil obtained from the roots of *Panax ginseng* is used for exhibiting anti-alopecia activity. Ginsennosides are the active phytochemicals responsible for exerting anti-alopecia activity. They enhance hair growth through 5α -reductase inhibition. 5α -Reductase is an enzyme that produces dihydrotestosterone (DHT) from testosterone. DHT then combines with the androgen receptor and forms a complex that interferes with DNA replication and disrupts the protein that is responsible for hair growth. Hence, inhibition of 5α -reductase causes enhanced hair growth (Kaushik et al., 2011).

5. Sereno arepens (Fig. 14): Serenoa repens belongs to the family Arecaceae and the order Arecales. They are native to coastal plains of South Carolina to South-Eastern



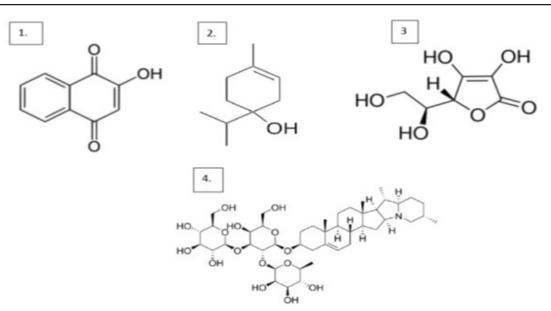


Fig. 11. Structure of phytochemicals showing anti-dandruff activity: 1. Lawsone, 2. Terpinen-4-ol, 3. Ascorbic acid, 4. Saponins.



Fig. 12. Botanicals showing anti-dandruff activity: 1. *Lawsonia inermis* L., 2. *Melaleuca alternifolia*, 3. *Sapindus mukorossi* Gaertn, 4. *Acacia concinna* Linn.



Louisiana including the Florida peninsula and are wellgrown in prairies, scrub, maritime forests, swamps and sandy dunes. The oil obtained from the berries is used for exhibiting anti-alopecia activity. Phytosterol and steroidal saponins are the phytochemicals responsible for the anti-alopecia activity. Phytosterol comprises 2.04 mg/g of total phytochemicals (Penugonda and Lindshield, 2013) which enhances hair growth by blocking DHT activity. It also blocks the formation of dihydrotestosterone (DHT) and prevents the disruption of proteins responsible for hair growth. Hence, blocking of DHT causes enhanced hair growth (Kaushik et al., 2011).

2.7.3. Anti-lice

Head lice are obligatory ectoparasite which complete their entire life cycle on the scalp. Head lice infestation is caused by Pediculus humanus capitis and is referred to as hematophagous that survives by sucking the blood. The transmission may be direct, i.e. from one head to another or indirect, i.e. through hairbrushes, bedding, blankets and common use of the wardrobes. The main reason for their occurrence is unhygienic living conditions. The infestation is followed by itching, irritative allergic reactions which are the results of deposition of the saliva of the insects on the scalp. The main outcome of head lice is scalp pruritus (Di Campli et al., 2012; Kanlayavattanakul and Lourith, 2018).

The most common botanicals used for the treatment of head lice are:

1. Melaleuca alternifolia (tea tree): The active phytochemicals present are terpinen-4-ol, α-terpeninol, linalool, etc. They exert antiseptic and pediculocidal activity (Di Campli et al., 2012).

2. Azadirachta indica A. Juss (Neem): It belongs to the family of Meliaceae and order Rutales. They are widely distributed to dry areas like Afghanistan, Pakistan, India, Sri Lanka, Bangladesh, Myanmar and China, particularly in the tropical and semi-tropical regions. Neem extracts obtained from the relevant seeds are used as oil or shampoos for treating lice. Azadirachtin (Fig. 15) is the most active phytochemical responsible for blocking the action of insect molting hormone, named ecdysone. In this way, it provides a pediculocidal activity (Metcalf, 2000). The amount of azadirachtin in neem extracts ranges from 0.2 to 0.4%. Also, azadirachtin shows an antiseptic property (Elteraifi and Hassanali, 2011).

3. Tanacetum cinerariifolium TREV. (Pyrethrum) (Fig. 16): Pyrethrum belongs to the family Asteraceae and order Asterales. They are native to Asia and North-Eastern Europe and are well-grown in rocky ground, usually by the seashore. The active insecticidal phytochemicals called pyrethrin are highly present in the flower heads which ranges from 24.5 to 25.5% (Ujváry, 2010). Pyrethrum extract obtained from flower heads is used as cosmeceutical in the form of shampoo, oil, etc. From a mechanistic point of view, pyrethrin functions as sodium channel (Na⁺⁾ blocker which delays repolarization leading to paralysis in lice; thereby preventing them from feeding which result in the eradication of lice (Silver et al., 2014).

belongs to the family Myrtaceae and order Myrtales. They are well-distributed throughout Australia and are well-grown in coastal sites, closed forests, dry inland regions ranging from well-drained to poorly drained, acid to alkaline and sandy soils to rocky clay loamy soil. The eucalyptus extract is obtained from its leaves and is available in the form of oil for the treating lice. The major phytochemical responsible for strong odor is 1,8-cineole which comprises of 48.5% of leaves and acts as an insect repellent and shows remarkable ovicidal activity (Soonwera et al., 2018).

5. Pongamia pinnata L. Pierre (Indian beech): Indian beech belongs to family Fabaceae and order Fabales. It is native to India and South-east Asia and is well-grown in humid tropical areas containing red soil or black soil with an altitude of approximately 1,200 m, annual rainfall of 500 to 2,500 mm and temperature ranges from 28 °C to 40 °C.

The extracts are obtained from leaves and seeds and are available as cosmeceuticals in the form of oil (Yadav, 2011) (Lice 1). The various phytochemicals of P. pinnata are flavonoid derivatives, e.g. flavones, flavans and chalcones), sesquiterpene, diterpene, triterpenes, steroids, amino acid derivatives, disaccharide, fatty acids and esters. This plant species has pediculocidal as well as ovicidal activity. It was reported that the petroleum ether extracts of P. pinnata L. Pierre possess an excellent anti-lice activity with values ranges from 50.3 to 100% as compared to chloroform and methanol extracts and acts as an active anti-louse agent (Yadav, 2011).

2.8. Extraction procedures

Extraction is an important step in the analysis of medicinal plants, since through the extraction; the desired chemical components from the plant organs are obtained which further undergo separation and characterization. Before extraction, the collection of correct plant organs plays an important role in the preparation of cosmeceuticals. Collection of plant part depends upon the content of the interested active phytochemicals on the plant part, the growth stage of the plant, harvesting season, method of handling during collection and the physical condition of the collection place. The basic steps involved in the preparation of sample for extraction consist of pre-washing, drying of plant material, grinding of plant material to provide a homogenous sample and to increase the contact of sample surface with the solvent system. The selection of solvent system depends on the specific nature of the targeted bioactive phytochemical(s). Polar solvents like methanol, ethanol or ethyl-acetate were used for extracting hydrophilic compounds, whereas dichloromethane or a mixture of dichloromethane/ methanol in ratio of 1:1 was used for the extraction of lipophilic compounds (Sasidharan et al., 2011). The other solvents employed for the extraction of phytochemicals are chloroform, distilled water, acetone, n-hexane, petroleum ether (Ngo et al., 2017), acetonitrile, toluene, isopropanol, ethylene glycol, propylene glycol, 2-butanol, 1-pentanol, ni-



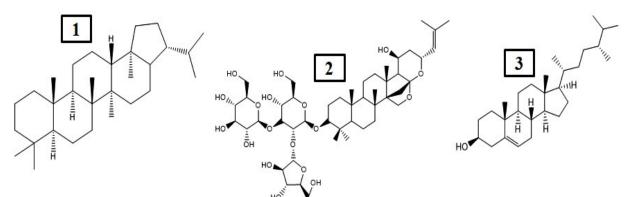


Fig. 13. Structure of phytochemicals showing anti-alopecia activity: 1. Triterpenoids, 2. Bacosides, 3. Polysterols.



Fig. 14. Botanicals used in treating hair fall: 1. Bacopa monnieri L. 2. Sereno arepens.

tromethane, tetrahydrofuran, cyclohexane, cyclohexanone, pyridine dichloromethane, butanone, methyl acetate, butyl acetate, carbon disulphide, octanol, isobutanol and amyl acetate (Bergs et al., 2013). The various techniques for extraction included maceration, infusion, digestion, percolation, decoction, hot continuous extraction (Soxhlet), aqueous-alcoholic extraction by fermentation, sonication, counter current extraction, microwave-assisted extraction, supercritical fluid extraction, accelerated solvent extraction (ASE), and distillation, etc. Plant extracts generally occur as a combination of various types of phytochemicals, so, for obtaining a desired or targeted bioactive agent, various separation techniques were adopted after extraction. The different separation techniques were adsorption column chromatography, liquid chromatography partition chromatography, counter-current chromatography, gel filtration chromatography, TLC, column chromatography, flash chromatography, high-resolution GC/MS (HRGC/MS), ion exchange chromatography, HPLC/MS, HPLC/MS/MS and tandem MS (MS/MS), gas chromatography, superficial critical chromatography, sephadex chromatography, molecular distillation, capillary electrophoresis and HPLC. Besides chromatographic techniques, there were certain non-chromatographic techniques like immunoassay, phytochemical screening assay and Fourier-transform infrared spectroscopy (FTIR) (Zhang et al., 2018). HRGC/MS and GC-FID are considered as the modern methods of choice for separation of volatile and non-volatile components such as essential oils (Ong, 2004; Nwiloh et al., 2016). Liquid chromatography (LC) with an isocratic/gradient elution, HPLC and its derivatives are the techniques chosen for the separation of thermally labile botanical and herbal constituents. Capillary electrophoresis was a powerful alternative of HPLC for isolation and

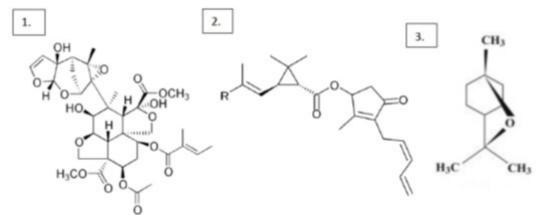


Fig.15. Structure of phytochemicals showing anti-lice activity: 1. Azadirachtin, 2. Pyrethrin, 3. 1,8-Cineole.



Fig.16. Botanicals showing anti-lice activity: 1. Azadirachta indica A. Juss, 2. Tanacetum cinerariifolium TREV, 3. Eucalyptus globulus Labill, 4. Pongamia pinnata L. Pierre.

purification of polar and thermally labile compounds. HPLC/MS was also capable of isolating and purifying of thermally labile compounds ranging from small polar molecules to macromolecules involving proteins, carbohydrates, nucleic acid, etc. (Ong, 2004). Hence, it was concluded that chemical analysis played a vital role in the development and characterization of botanical and herbal preparations. The use of all these validated techniques and methods enables us to enhance the quality of the product obtained after extraction.

2.9. Importance of medicinal plants in a variety of scientific disciplines

Since ancient times, medicinal plants have undoubtedly been recognized by human beings for their eminent activities in the field of medical care that range from the development of new medicines to vaccinations (Jamshi-



4. *Eucalyptus globulus* Labill. (Eucalyptus): *Eucalyptus* di-kia et al., 2018). The phytochemicals are of primary importance in various fields of pharmaceutical, chemical, botanical, medicinal and traditional medicines. The medicinal and health-promoting activities are generally related to the phytochemicals present in their secondary metabolites (Venditti et al., 2018). These phytochemicals are essential oils, terpenes, alkaloids, tannins, flavonoids, amides, glycosides, fatty acids, vitamins, carbohydrates, etc. The examples of these phytochemicals in various disciplines are summarized in Table 2.

2.10. Toxicity of botanicals

Herbal cosmeceuticals were said to be free from side effects. However, it was later found to be a myth (Fatima, 2016). Some examples showed that well-known botanicals contained some phytochemicals which are toxic and poisonous and can cause adverse side effects. Some examples of such botanicals were listed in the Table 3.

2.11. Regulation and safety

FDA has imposed stringent inspection requirements for the approval of drugs but no such requirements have been imposed in the case of cosmetics. In fact, cosmeceuticals are the borderline products that exist between cosmetics and pharmaceuticals. The Federal Food, Drug and Cosmetics Act and FDA do not recognize "cosmeceuticals"; however, the aesthetic and functional benefits of these products are enjoyed after becoming over the counter drugs (Kaul et al., 2018). There are three categories of products in the US according to USFDA, namely cosmetics, drugs and OTC drugs and no such legal definition was available specifically for "cosmeceuticals". The classification of products in USFDA mainly depends on the claims of the products (Raj and Chandrul, 2016). In Japan, the "cosmeceuticals" are called "quasi-drugs" as it falls between cosmetics and drugs. According to the regulatory system of Japan, the ingredients must be preapproved before incorporating them into the quasi-drugs as well as before selling them in the market (Kaul et al., 2018). In Australia, goods are categorized based on claims made on the products and their compositions. In Australia, borderline products are called "therapeutic goods" and are registered by the Australian Register of Therapeutic Goods. Accordingly, only approved ingredients are allowed for the manufacturing of "therapeutic goods" (David, 2005). Cosmeceuticals are called "dermo-cosmetics" in Canada. They are not classified as an independent cosmetic category, instead, the Canadian health authorities have identified category V for the accommodation of those products falling under the category of both cosmetics and and drugs. It was stated that fewer regulatory requirements are enforced for the regulation of these types of products. In European Union, cosmetics are regulated under Cosmetic Directive 76/768/EEC but do not have any regulations regarding the category called "cosmeceuticals", however, it does impose certain stringent

laws in which the submission of proofs are required for any claims made by the company (Tripathy and Dureja, 2015). In China, cosmeceuticals are called "cosmetics for special use." According to China FDA (CFDA), "cosmetics for special use", undergoe various safety and health quality tests like microbiology, toxicology, chronic toxicity and carcinogenic tests along with conducting safe trials for human use. Thus, it was reported that according to CFDA, imported cosmetics are categorized into two categories, namely ordinary cosmetics and special use cosmetics. Both types of cosmetics require a different type of license from State Food and Drug Administration (SFDA) and for marketing, hygiene license or record-keeping certificate must be obtained from the Health Administration Department of the State Council-SFDA (Kaul et al., 2018).

2.12. Marketed herbal cosmeceuticals

The various herbal cosmeceuticals marketed globally were listed in Table 4.

2.13. Nanotechnological approaches in cosmeceuticals

Nanotechnology manifests the advancements in the field of research and development, by improving the efficacy of the product through delivery. To overcome certain limitations associated with the conventional products, the application of nanotechnology is expanding in the area of cosmeceuticals. Nanocosmeceuticals used for skin and hair conditions like wrinkles, acne, photoaging, hyperpigmentation, dandruff, alopecia and hair damage, have come into widespread use. The various nanocarriers like liposomes, niosomes, nanoemulsions, microemulsion, solid lipid nanoparticles, nanostructured lipid carriers and nanoparticles were used in place of the conventional delivery system. These novel nanocarriers exhibit various advantages over conventional systems like enhancing skin penetration, controling and sustaining drug release, higher stability, site-specific targeting and high entrapment efficiency (Kaul et al., 2018). For the efficient delivery of nano-cosmeceuticals, various nanocarrier technologies have been employed which offered an inventive approach for the delivery of active phytochemicals. Various novel nanocarriers for delivery of herbal cosmeceuticals are shown in Fig. 17. 1. Liposomes: Liposomes are the vesicular structures with aqueous core, enclosed by a lipidic bilayer. The main component of lipidic bilayer is phospholipids. The phytochemicals are entrapped within the liposomes to protect them from metabolic degradation and to release them in a controlled manner. They are suitable for the delivery of both lipophilic as well as hydrophilic phytochemicals. Their size ranges from 20 nm to several micrometers. Phytochemicals like vitamins A, E, K, carotenoids, lycopene, CoQ10, etc. have been incorpo rated within the liposomes, which further amplify their physical and chemical stability. Liposomes are used in antiaging creams, moisturizing cream, sunscreen, beauty creams and also in the treatment of hair loss (Kaul et al., 2018). Based on this concept, Dior developed



Medicinal plants in different disciplines.

Plants	Phytochemicals	Disciplines	References	
	Fatty a	cids	<u>.</u>	
	α-Linolenic acid	Cardioprotective		
Styrax officinalis	Linoleic acid	Antioxidant	Venditti etal ,2018	
	Terpe	nes	•	
Styrax officinalis	Egonol	Antiasthmatic, cytotoxic, antifungal and antibacterial	Venditti etal., 2018	
Achillea millefolium L.	1,8-Cineole, sabinene, trans- sabinenehydrate, camphor, borneol	Expectorant, anti-infection, astringent, antidiabetic, antispasmodic, anti-dandruff and antipyretic	Mohammadhosseini et al., 2017	
	and lavandula	anti-Inflammatory and carminative		
Azadirachta indica A. Juss.	γ-Elemene	Antitrypanosomia	Wansi etal. ,2019	
Allium cepa	Diallyl trisulfide and dipropyltrisulfide	Acetylcholinesterase inhibitory	Wansi etal., 2018	
Piper guineense	Limonene and β-caryophyllene	Anxiolytic effect	Wansi etal., 2019	
Linalool and 3,5-dimethoxytoluene		Sedative		
	Este	rs		
	Benzoyl ester and benzoates	Food preservatives	Venditti etal., 2018	
Styrax officinalis	Glutamic acid	Flavor enhancer		
	Alkalo	ids		
Erythroxylum coca	Cocaine	Local anesthetics and cerebral stimulant		
Papver somniferum	somniferum Morphine Analgesics]	
Piper nigrum L.	Piperidine	Bactericidal	Chikezie et al., 2015	
Camptotheca acuminata	Camptothecin	Anti-cancer		
Rauwolfia serpentina				
	Flavon	oids		
Moringa oleifera	Quercetin	Anti-inflammatory, anti-hypertensive and antibacterial	Vergara-jimenezet al., 2017	
Silybum marianum L.	Silibinin, silydianine and silychristine	Hepatoprotectant	Kshirsagaretal., 2009	
Artemisia giraldi	6,7,4-Trihydroxy-3,5-dimethoxyflavone	Anti-microbialactivity	Chikezie et al., 2015	
Vitis vinifera L.	Naringenin	Improves hyperlipidemia and hyperglycaemia	Chikezie et al., 2015	
Ziziphora clinopodioides Lam.	Thymonin, chrysin, acacetin and apigenin	Spasmolytic	Mohammadhosseini, 2017	

"Capture", a liposomal antiaging cream in the year 1986 (Duarah et al., 2016) and various researches are currently working on liposomes for the delivery of cosmeceuticals. Recently, curcumin-loaded liposomes were formulated that showed enhanced skin protection activity (Ganesan and Choi, 2016).

2. Nanogel: Nanogels are crosslinked, sub-micrometer sized particles of hydrophilic polymers and are highly soluble in water. Researchers at Columbia University, New York have synthesized nanogels that were comprised of nanosized cross-linked particles and have vast amounts of interstitial spaces. Active encapsulation showed that nanogels provided enhanced binding which further offered an improved time-release application. Hence, it can be used in cosmeceuticals for improved delivery of active phytochemicals (Kaur and Agrawal, 2008).

3. Niosomes: Niosomes are bilayer vesicles that are formed by self-assembly of non-ionic surfactants, with or without cholesterol or their lipids. They are widely

used in cosmeceuticals because they have multiple advantages over liposomes like higher stability, enhanced skin penetration and low toxicity (Ganesan and Choi, 2016). Their size ranges from 100 nm to 2 μ m in diameter. Various niosomal cosmeceuticals were available to the market like antiwrinkle creams, skin whitening and moisturizing cream, hair repairing shampoo, conditioner, etc. (Kaul et al., 2018). Recently, a niosomal formulation of resveratrol, alpha-tocopherol and curcumin was produced that showed increased antioxidant activity with increased skin permeation efficacy (Ganesan and Choi, 2016).

4. Solid Lipid Nanoparticles (SLN): Solid lipid nanoparticle (SLN) is a lipid-based system comprising of the lipidic core with size ranges from 50 to 1000 nm. SLN can incorporate both lipophilic and hydrophilic active ingredients. SLNs are used in cosmeceuticals because they are composed of biodegradable and physiological lipids that exhibit less toxicity. Their small size ensuresclose contact with the skin which increases the pene-



Toxicity/adverse effects of so	me botanicals.
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S.No.	Botanicals	Toxicity dose/ concentration	Toxicity/Adverse effects	Phytochemicals responsible	Application Field	Ref.	
1	Glycyrrhiza glabra L	> 600 mg	Hypokalemia, hypertension, and myopathy	Glycyrrhizin and glycyrrhetinic	Anti- inflammatory	Tovar and Petzel, 2009	
			Cardiac Arrhythmias.	acid			
2	<i>Ephedra sinica</i> Stapf	20-60 mg	Hypertension, myocardial infarction, seizure, stroke, and psychosis	Ephedrine	Improves skin conditions	Tovar and Petzel, 2009	
3	Mentha pulegium	≥ 5 mL	Hepatotoxic and seizures	Pennyroyal oil	Antiseptic	Tovar and Petzel, 2009	
4	Angelica senensis	> 100 mg	Skin irritation, sun sensitivity, bruising and bleeding	Ferulic acid and ligusticide	Wound treatment (Skin rejuvenate)	Tovar and Petzel, 2009	
5	Aloe barbadensis Miller	≥ 50 ppm	Electrolyte depletion	Anthrones	Anti- inflammation, protection from sunburn.	Tovar and Petzel, 2009	
			Overdose can cause	Atropine,	Anti dandruff		
6	Datura stamonium L.	≥ 100 mg	acute anticholinergic toxicity and death	L-Hyoscyamine and L-scopolamine	Anti-dandruff, anti-hair fall	Tovar and Petzel, 2009	
7	Eucalyptus globulus Labill.	3.5 mL oil	Seizures	Cineole	Expectorant	Tovar and Petzel, 2009	
8	Ginkgo biloba	240 mg	Severe allergic reactions	Ginkgolic acid	Anti- inflammatory	George, 2011	
9	Silybum marianum L.	≥ 0.2%	Cerebral hemorrhage, hepatic coma and neuropathy	Silymarin	Antioxidants	George, 2011	
10	Hypericum perforatum	> 0.3%	Neuropathy and photosensitivity	Hypericin	Anti- inflammation, skin- protectants against burns and wounds	Tovar and Petzel, 2009	

tration of active phytochemicals through the skin. Also, they have an intrinsic UV resistant property. In addition to these, SLNs provide an occlusive property which increases the skin hydration and keeps the skin moist and hydrated. Recently, in the field of cosmeceuticals, vitamin A-loaded SLNs were constructed which increased the skin moisture retention and provided an occlusive effect over the skin. Similarly, caffeine-loaded SLNs were constructed which enhanced the permeation efficacy of caffeine across the skin and showed increased skin protection (Ganesan and Choi, 2016).

5. Nanocapsules: Nanocapsules comprise of a liquid or solid core which encloses the active component and is further coated by a polymeric membrane of natural

or synthetic polymers. Their size ranges from 10 nm to 1000 nm (Duarah et al., 2016) and shows improved effects on the delivery of phytoactive compounds for the development of cosmeceuticals. Recently, resveratrol and curcumin loaded lipid core nanocapsules were formulated which provided an increased retention of polyphenols in the skin and offered enhanced skin protection. Similarly, chitosan-capsaicinoids combined nanocapsules were developed which showed controlled release of the phytochemicals and provided increased skin protection (Ganesan and Choi, 2016). 6. Nanostructured Lipid Carriers (NLCs): Nanostructured lipid carriers are the second-generation lipid nanocarri-ers, developed to overcome the drawbacks associated



Marketed herbal cosmeceuticals.

Herbs Marketed products					
I. Antioxidants					
1. Green tea	Celestial seasonings antioxidant green tea				
2. Pomegranate	Pure beauty pomegranate antioxidant serum				
3. Mushroom	Purica Chaga micronized mushroom antioxidant support				
	II. Sunscreens				
1. Aloe vera	Jovees Aloe Vera and Chamomile Sunscreen with SPF 25				
2. Green tea	W- Lab Natural Green Tea Sunscreen				
3. Gambir Clé de Peau Beauté UV protection emulsion SPF 50+					
III. Anti-inflammatory agents					
1. Aloe Ali Express Aloe Vera gel anti-inflammatory cream					
2. Mushroom Real herbs Reishi mushroom extract dietary supplement					
3. Silybin	Naturaheal Silymarin 300 (milk thistle)- capsules				
4. Turmeric	Bodhi tree naturals turmeric anti-inflammatory balm				
	IV. De-pigmenting agents				
1. Citrus fruits Biotique bio fruit whitening and depigmentation face pack.					
2. Rice	100% pure fermented rice water toner				
3. Ginseng	Natural Republic Ginseng royal silk cream				
	V. Skin renewal agents				
1. Aloe Vera	Himalaya Herbals Anti-wrinkle Cream				
2. Aloe Vera	Lotus herbals aloe hydra moisturising gel				
3. Carrot	Makari extreme carrot and argan oil toning cream				
4. Coconut oil	Spa naturals coconut oil moisturizing cream				
5. Basil Body Dear basil anti-acne and anti-pimple cream					
	VI. Anti-dandruffagents				
1.Henna,lemon Dabur Vatika Henna and lemon anti-dandruff shampoo.					
2.TeaTree	Jovees thyme and tea tree anti-dandruff shampoo				
3. Lemon	Soul Tree anti-dandruff shampoo with aloe and lemon peel				
4. Reetha	Lotus Neemactiv neem and reetha antidandruff shampoo.				
6. Shikakai	Eeshha herbal anti-dandruff hair oil with shikakai and fenugreek				
	VII. Alopecia				
1. Ginseng	Jovees Henna and Ginseng anti-hair loss shampoo				
2. Amla,Brahmi	VLCC Ayurveda anti-hair fall shampoo				
3. Green Tea	Follow me green tea anti-hair fall shampoo				
4. Aloe Vera	Parachute advanced aloe vera enriched coconut hair oil				
5. Onion	Kazima onion herbal shampoo				
6. Lavender	Organic lavender botanicals anti-hair loss conditioner				
	VIII. Anti-liceagents				
1. TeaTreeoil	Reitzer pharmaceuticals treet-It tea tree oil anti-lice gel cream				
2. Neem	Medikar anti-lice treatment shampoo with coconut oil and neem				
3. Pyrethrum	Natural look anti-lice pyrethrum regimen oil				

with SLN (Kaul et al., 2018). They entrap several phyto-active compounds.

Recently, quercetin-loaded NLCs were constructed that showed increased topical delivery of phytochemicals and enhanced antioxidant activity. Similarly, squalene-enriched NLC was developed for the treatment of hair follicles against Alopecia areata (Ganesan and Choi, 2016). 7. Nanoemulsion: Nanoemulsions are kinetically and thermodynamically stable dispersion of the oil phase in the water phase in combination with surfactants. Their size ranges from 50 nm to 200 nm. Nanoemulsions used for S are



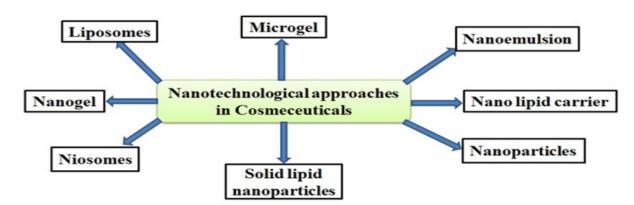


Fig. 17. Various types of nano-carriers used for delivery of herbal cosmeceuticals.

cosmeceuticals like sunscreens, shampoos, lotions, conditioners and hair serums (Kaul et al., 2018). Recently, quercetin-loaded nanoemulsions were prepared which showed increased skin retention of quercetin and hence exhibited enhanced antioxidant activities (Ganesan and Choi, 2016).

8. Microgel: Microgels are nanosized cross linked particles synthesized by polymerization. Due to their open network-type structure, microgels provided large surface areas and are used as carriers of phytochemicals (Kaur and Agrawal, 2008).

Some examples of phytoactive compounds loaded nano-cosmeceuticals used in skin and hair care are listed in Table 5.

2.14. Patents

As the popularity of nanotechnology is increasing in the recent scenario, the number of patents is also increasing by 30% every year since 2000. Over 5000 nanotech-related patents are being issued in the late March 2006 in the USA. The highest patent filing was observed in the field of nanoparticle (147% since 2000) followed by nanotube (141%) and fullerene (139%). Between 2000 and 2005, the maximum number of patent filing was performed by the USA followed by China and then Japan. Recent findings showed that Europe is also growing in this field, as represented by Germany and France. During the late March 2005, 3,818 US nanotech patents were being issued and about 1,777 patents are waiting for their judgment. Some examples of nano-tech patents are listed in Table 6 (Kaur and Agrawal, 2008).

4. Concluding remarks

The application of cosmeceuticals has increased in recent years in the field of skin care and hair care to overcome the skin and hair-related problems. The global trend in the cosmeceutical industries for developing 'medicinally' active cosmetics or 'cosmetically' oriented medicinal products became a part of the current 'lifestyle' ideology. Cosmeceuticals like vitamins, retinols, hydroxyl acids of which many are used in treating skin and hair related problems, considerably improve skin and hair conditions. In the present study, several plants belonging to different families were identified that are used by the people to cure and improve dermatological disorders and conditions respectively, prevent hair damage and also used as cosmetics. It was further found that combination of new vehicles and delivery systems with established ingredients altered the percutaneous absorption and provided a good safety curative profile. The greater demand for the application of nanosized active phytochemical in the development of nano-cosmeceuticals led to many researches in the field of novel nano-cosemecutical-based therapy. The various nano-cosmeceutical-based therapies for skin care and hair care include moisturizing, sun blocking, anti-aging, whitening effects, anti-dandruff, anti-hair fall etc. Over the next 5 years, the most influential angle in the field of cosmeceuticals will be the establishment of links between the internal health and the beauty.

Conflict of interest

The authors declare that there is no conflict of interest.

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Phyto-bioactive of	compounds	loaded	nano-cosmeceuticals.
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S.No.	Phytochemicals	Nano-deliverymethods	Application	References
1	Rice bran oil which contains tocopherols and gamma- oryzanol	Nanoemulsion	Moisturizers	Bernardi et al., 2011
2	Raspberry seed oil containing anthocyanin	Lipid nanocarriers	Sunscreen	Niculae et al., 2014
3	Lavender extracts containing polyphenols	Polymeric Nanoparticles	Anti-aging	Pereira et al., 2015
4	Rosemary extracts which contains flavonoid compounds	SLN	Antioxidants	Lacatusu et al., 2010
5	Aloe vera extracts containing aloesin	Liposomes	Skin care	Takahashi et al., 2009
6	Safflower extracts containing safflower yellow	NLC	Hair care	Kumar et al., 2011
7	D-limonene	Nanoemulsion	Skin care	Lu et al., 2014
8	Quercetin	NLCs	Skin care	Guo et al., 2012
9	Hinokitiol	Nanocapsules	Hair care	Hwang and Kim, 2008
10	Propolis and lycopene	Nanoemulsions	Skin care	Butnariu and Giuchici, 2011

Table 6

Examples of patent herbal nano-cosmeceuticals.

S.No.	Trade name	API	Use	Company	Technology
1	Bioperformance Crème Super Régénérante Absolute	Y-Linolenic acid	Skin care	Lancôme	Nanocapsules
2	Platinéum	Hydroxyapatite	Antiaging	Lancôme	Nanoparticles
3	Revitalift	Pro-retinol A	Anti-wrinkle	L'Oréal	Nanosomes
4	Rénergie Microlift	Micro filters	Antiaging and moisturizer	L'Oréal	Nanoparticles
5	NanoSal TM Moisture Key	Sodium acetylated hyaluronate, ceramides and shea butter and glycerine	Moisturizer	Salvona	Solid hydrophobic nanospheres
6	Royal Jelly Lift Concentrate	Royal Jelly	Anti-wrinkle	Jafra Cosmetics	Liposomes

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