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Arabian medicinal plants with dermatological effects- plant based review (part 1)

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Abstract: Several medicinal plants possessed a wide range of dermatological effects included antibacterial, antifungal, antiviral, antiparasitic, anticancer, hair growth-promoting activity, wound healing effects, for the treatment of burns, eczema, acne, vitiligo, and psoriasis, as skin lightening, as skin protection therapy and to slow down skin ageing. The current review will discuss the medicinal plants which showed dermatological effects and applications.

Keywords: medicinal plants, skin, dermatology, alternative medicine, complementary medicine

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I. INTRODUCTION:

Human skin, the outer covering of the body, is the largest organ in the body. It also constitutes the first line of defense. Skin disease is a common ailment and it affects all ages from the neonate to the elderly and cause harm in number of ways. The skin diseases can be categorized into nine common types: rashes, viral infections, bacterial infections, fungal infections, parasitic infections, pigmentation disorders, tumors and cancers, trauma and Other conditions such as wrinkles, rosacea, spider veins and varicose veins which cannot be neatly categorized[1]. Several medicinal plants possessed a wide range of dermatological effects included antibacterial, antifungal, antiviral, antiparasitic, anticancer, hair growth-promoting activity, wound and burn healing effects, for the treatment of eczema, acne, vitiligo, and psoriasis, as skin lightening, as skin protection therapy and to slow down skin ageing[2-10]. In the current review, the medicinal plants which showed dermatological effects and applications were reviewed.

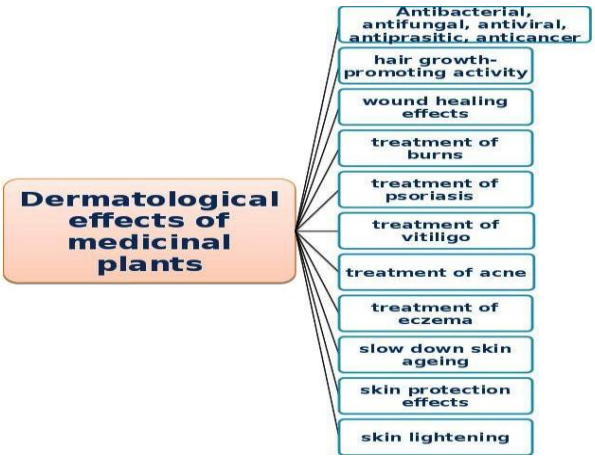

Fig 1: Dermatological effects of medicinal plants

Wounds and burns healing effects:

Wounds healing:

Agrimonia eupatoria

Prepared ethanolic extract ointment showed wound healing activity in rats in contrast with fucidin ointment and aqueous extract ointment, hence the wound healing was completed in l0 days by using the ethanolic extract ointment, while the healing was completed in 12 and 14 days for the aqueous extract and fucidin ointments respectively, in comparison with the untreated wound which needed more than 16 days for healing completion [11-12].

Allium sativum

A randomized placebo-controlled double-blinded study show that 5 h after the administration of garlic powder a significant increase in capillary skin perfusion occurs by 55% in the healthy volunteers. The increased erythrocyte velocity results from vasodilation of precapillary arterioles which increases diameter of erythrocyte column by an average of 8.6% [13]. Chicken skin wounds exposed to aged garlic extract show an increase in the re-epithelialization and dose-dependent neovascularization [14-15].

Aloe vera

Aloe vera gel enhanced wound healing. It reduced wound diameter (induced on both sides of the vertebral column) by 62.5% in mice receiving 100 mg/kg/day orally and 50.80% in animals receiving topically 25% *Aloe vera* [18]. Many studies showed that aloe hasten wound healing cause by burns, frostbite, electrical injuries, caustic chemicals and surgery. It stimulated the activity of macrophages and fibroblasts which increase both collagen and proteoglycan synthesis and promote tissue repair**.** It also enhanced collagen deposition and cross-linking in granulation tissue in wounds and improved scar strength compared with topical antibiotic medication [19-22]. Acemannan also accelerated wound healing and reduce radiation induced skin reactions [16-18].

Ammannia baccifera

The application of leaf extracts of *Ammannia baccifera* L cream to the infected wound in rats, it improved the healing activity and reduced the risk of further infection. The application of ethanolic leaf extracts of *A. baccifera* was found to improve the different phases of wound repair, including collagen synthesis and maturation, wound contraction and epithelialization [19-20].

Bauhinia variegata

Excision and incision wound models in albino Wistar rats, were used to evaluate the wound healing activity of the ethanolic and aqueous extracts of root of *Bauhinia variegata* at dose of 200 and 400 mg/kg bw. Both aqueous and ethanolic extracts of root of *Bauhinia variegata* at both doses produced significant wound healing by excision and incision wound models, which was comparable to that of standard (framycetin) in excision wound model [21-22].

Bellis perennis

The wound healing activity of *Bellis perennis* flowers was evaluated in Wistar albino rats. Dried *Bellis perennis* flowers were extracted with ethanol, then fractioned with n-butanol and an ointment was prepared from the n-butanol fraction. Six wounds were created for each animal by using circular excision wound model. The first two wounds were treated topically with HOTBp (hydrophilic ointment treatment containing n-butanol fraction). The second two wounds were control group and not treated with anything. The third two wounds were treated only with HOT (hydrophilic ointment treatment without n-butanol fraction). Treatments were applied once a day and lasted for 30 days. Wound samples were excised on days 5th, 10th and 30th. The percentage of wound healing was calculated by Walker's formula after measurement of the wound area and the tissue samples were examined histopathologically. The percentages of wound closure (HOTBp: 100%; HOT: 85% and control: 87%) and histopathological observations showed that there were statistically significant differences between HOTBp, HOT and control groups ($p < 0.05$) at 30th day. The authors concluded that topically administered ointment prepared from the n-butanol fraction of *Bellis perennis* flowers has a wound healing potential without scar formation in circular excision wound model in rats [23].
Bellis perennis is the homeopath's first choice for deep tissue injury, it is also one of the top remedies for joint and muscular soreness, deep tissue injuries and sport occidents [24-25].

Bryophyllum calycinum

The ethanolic extract of the leaves of the plant was evaluated for its wound healing activity by using excision wound model in rats. The histological investigation showed that plant leaf ethanolic extract exhibited significant wound healing potential which could be attributed to the presence of steroid glycosides [26-27].

Caesalpinia crista

The wound healing activity of different extracts of seed kernels of *Caesalpinia crista* was investigated in excision, incision and dead space wound models in albino rats. Ethyl acetate fraction of seed kernel of *Caesalpinia crista* has shown better wound healing activity in all models as compared to alcoholic extract and ether fraction. While petroleum ether extract, butanol fraction and butanone fraction has shown the least effective wound healing activity [28-29].

Calendula officinalis

The effects of oral and topical application of *Calendula officinalis* flower extract on excision wounds were checked in rats. The percentage of wound closure was 90.0% in the extract-treated group, whereas the control group showed only 51.1% on the eighth day of wounding ($P<0.01$). The days needed for re-epithelization were 17.7 for the control animals; while, extract treatment at a dose of 20 or 100 mg/kg bw reduced the period to 14 and 13 days, respectively. A significant increase was observed in the hydroxy proline and hexosamine content in the extract-treated group compared with the untreated animals [30].

Surgically induced skin wounds in rats were treated with a 5% Calendula ointment in combination with allantoin. The drug combination was found to markedly stimulate physiological regeneration and epithelialization. This effect was attributed to more extensive metabolism of glycoproteins, nucleoproteins and collagen protein during the regenerative period in the tissues [31-32].

Calendula officinalis

The therapeutic efficacy of marigold (*Calendula officinalis*) extract was investigated in the epithelialization of lower leg venous ulcers. Twenty-one patients with 33 venous ulcers out of 34 patients were treated with (*Calendula officinalis* ointment) which applied twice a day for 3 weeks. The second group was a control group that consisted of 13 patients with 22 venous ulcers. In the control group, saline solution dressings were applied to ulcers for the same period. In the experimental group the total surface of all the ulcers at the beginning of the therapy was 67,544 mm2. After the third week the total surface of all the ulcers was 39,373 mm2 (a decrease of 41.71%). In seven patients, complete epithelialization was achieved. In the control group the total surface of all the ulcers at the beginning of the therapy was 69,722 mm2. After the third week the total surface of all the ulcers was 58,743 mm2 (a decrease of 14.52%). In four patients, complete epithelialization was achieved. There was a statistically significant acceleration of wound healing in the experimental group ($p < 0.05$) [33].

Calotropis procera

The wounds healing effect of the latex of *Calotropis procera* was evaluated in rabbits. Animals were treated daily for 21 days. The wounds' diameters were measured on the day of wound creation, thereafter on days 7, 14 and 21 post wound creation. Biopsies of the wounds were taken on days 3 and 21 and viewed histologically. The wounds were found to be significantly ($p<0.05$) reduced in groups treated with 50% latex in honey and triamcinolone, on day 7 post wound creation, while there was a significant ($p<0.05$) reduction in wound surface area in all treated groups on days 14 and 21 post wound creation. Histological findings in untreated group showed thick bundle of collagen fibres some of which had broad based configurations, reminiscent of keloid. The group treated with 2ml of Calotropis latex revealed the presence of florid granulation tissues on day 3, while there was a marked reduction in quantity and size of collagen fibres on day 21 post wound creation which was comparable with what was seen for the triamcinolone-treated group [34-35].

Mice topically treated with Calo-protein, purified from the aqueous extracts of *C. procera* revealed antibacterial activity and significant wound healing after 14 days comparable to fusidic acid as positive control. This protein was devoid of cytolytic effect even at higher concentrations on skin cells after 24 h [36-37].

Cassia occidentalis

The wound healing property of methanolic crude extract of *Cassia occidentalis* leaves and a pure compound chrysophanol isolated from it, was evaluated in excision, incision and dead space wound models. The parameters studied included rate of wound contraction and the period of epithelialization in excision wound model. Tensile strength in incision wound model and granulation tissue dry weight in dead space model were assessed along with histopathological examinations. Chrysophanol was found to possess significant wound healing property than methanol crude extract. This effect was evident by the decrease in the period of epithelialization, increase in the rate of wound contraction, skin breaking strength, granulation tissue dry weight content and breaking strength of granulation tissue. Histopathological study of the granulation tissue showed increased collagenation when compared to control group of animals [38-39].

Clitoria ternatea

The wound healing activity of *Clitoria ternatea* seed and root extracts was investigated using excision, incision and dead-space models in rats. *Clitoria ternatea* seed and root extracts significantly improved wound healing in excision, incision and dead-space models when administered orally by gavage as well as applied topically as ointment. These effects were comparable to that of cotrimoxazole ointment. The finding of the study also showed that *Clitoria ternatea* affected all three phases: inflammatory, proliferative and remodeling phases of wound healing [40].

The wound healing potential of standardized *Clitoria ternatea* leaf extract in terms of different enzymatic models, which are mostly associated with skin wound, was evaluated. The methanol extract and fractions were screened for its hyaluronidase, elastase, and matrix metalloproteinase-1 (MMP-1) inhibitory activity compared with standard oleanolic acid. The activity was rationalized through reverse phase high performance liquid chromatography (RP-HPLC) standardization of the extract and fractions with respect to its isolated biomarker taraxerol (yield 5.27% w/w). The extract showed significant ($P < 0.001$) hyaluronidase (IC_{50}) 18.08 ± 0.46 µg/ ml) and MMP-1 ($P < 0.05$) inhibition, but the elastase inhibition was insignificant (IC_{50} 42.68 ± 0.46 µg/ml). Among the fractions, ethyl acetate fraction showed significant ($P < 0.001$) inhibition of hyaluronidase (IC_{50} 28.01 ± 0.48 µg/ml) and MMP-1 ($P < 0.01$). The HPLC analysis revealed that the extract and the ethyl acetate fraction are enriched with taraxerol (5.32% w/w and 4.55% w/w, respectively) [41-42].

Cupressus sempervirens

The essential oils obtained from cones of *Cupressus* were evaluated for their wound healing and anti-inflammatory effects. *In vivo* wound healing activity was evaluated by linear incision and circular excision experimental wound models, assessment of hydroxyproline content, and subsequently histopathological analysis. The healing potential was comparatively assessed with a reference ointment Madecassol. Additionally acetic-acid-induced capillary permeability test was used to test the oil anti-inflammatory activity. The essential oils of *Cupressus sempervirens* var. *horizontalis* and *Cupressus sempervirens* var. *pyramidalis* did not show any significant wound healing effect [43-44].

Cydonia oblonga

The healing effect of quince seed mucilage on the skin lesions induced by T-2 toxin was studied in rabbits. Rabbits received 5, 10, and 15% mucilage treatment. A solution of T-2 toxin (83 mg/ml) in methanol was prepared and 12 µl were applied on skin twice with 24 h interval. On the day eight, erythema and inflammation with grown hairs were observed. The complete healing of the skin damage was recorded in rabbits treated by 10 and 15% guince seed mucilage. The proposed mechanisms of healing effects of quince seed mucilage were: preventing impaired protein synthesis by T-2 toxin, acting as an obstacle between T-2 toxin and skin along with reducing water evaporation and acting as antioxidant [45-45].

Cynodon dactylon

The wound healing activity of hydroalcoholic extract of *Cynodon dactylon* was evaluated by using excision wound model. The parameters included the rate of wound contraction and the period of epithelization in excision wound model. Herbal ointment was prepared using different bases and concentrations 7.5% and 10% compared with standard cipladine (povidone-iodine). According to the healing parameters, the topical application of hydrochloric extract of *Cynodon dactylon* promoted wound healing activity in excision model in rat [47].

Wound healing potential of *Cynodon dactylon* was evaluated in different experimental model such as excision wound healing model and Incision wound healing model in albino Wistar rats by using the gel preparation of aqueous and alcoholic extract. Alcoholic and aqueous extract gel showed significant increased in the rate of wound healing in excision model ($p<0.05$) and in excision model ($p<0.01$) [48].

The wound healing activity of flavonoid fraction of *Cynodon dactylon* was evaluated in excision wound in mice. The flavonoid fraction of *Cynodon dactylon* were applied externally daily on the excised wound area for 8 days. The flavonoid fraction facilitated the healing process as evidenced by increase in collagen and protein and decrease in lipid peroxide in granulation tissue [49-50].

Cyperus rotuntdus

The alcoholic extract of tuber parts of *Cyperus rotundus* was examined for wound healing activity as ointment in three types of wound models in rats (the excision, the incision and dead space wound model). The ointments showed considerable difference in wound closure time and tensile strength in all wound models as compared to standard drug, nitrofurazone ointment (0.2 % w/w) [51-52].

Datura fastuosa

The ethanolic extract of *Datura fastuosa* was evaluated for wound healing activity in Wistar albino rats using excision wound model. The extract was formulated as an ointment at two concentrations (5% and 10% w/w). Nitofurazone ointment (0.2%w/w) was used as standard. The parameters utilized for evaluation were percentage wound closure, mean epithelization time, hydroxyproline, DNA and protein level. The histopathological studies were also carried out on wound tissue. The result revealed that 10% w/w *Datura fastuosa* ointment exhibit significant wound healing activity comparable to that of the standard [53-54].

Daucus carota

The soft paraffin based cream containing 1%, 2% and 4% w/w of ethanolic extract of *Daucus carota* L. (EEDC) root was formulated and evaluated in wound healing activity on excision and incision wound models. Animals treated with topical EEDC cream formulation (1%, 2% and 4% w/w) showed significance decrease in wound area, epithelization period and scar width whereas rate of wound contraction significantly increased (P <0.01, P <0.001 and P <0.001 respectively) as compared to control group animals in excision wound model. In incision wound model there was significant increase (P <0.01 and P <0.001) in tensile strength, hydroxyproline and protein content of animals treated with topical EEDC cream formulation (2% and 4% w/w, respectively). Ethanolic extract of *Daucus carota* L. root cream when applied topically did not show any sign and symptoms of skin irritation [55-56].

Dodonaea viscose

The effect of ethanol extract and flavonoid rich fraction of *Dodonaea viscosa* was investigated on a simplified *in vitro* wound healing study. Cultured Keratinocytes (HACAT) were exposed to ethanol extract and flavonoid rich fraction at different concentrations for 48 hours. The resultant cellular proliferation was determined after 48 hours by MTT assay and calculated relatively to control. Flavonoid rich fraction of the *Dodonaea viscosa* induced a significant cell proliferation after 48 hours exposure, when compared to the control group. The flavonoids rich fraction of the *Dodonaea viscosa* has better efficiency in inducing cell proliferation than ethanol extract [57].

Ethanolic extract of dried leaves showed wound healing activity in excised and incised wound in rats. 10% extract treated excision wound were found to have faster rate of contraction and epithelization. Ethanol extract suspension and ointment induced significant wound response (breaking strength of skin, granuloma and wound contraction) and overcome the anti-healing properties of dexamethasone [58-59].

Echium italicum

In vivo the wound healing activity of Echium species was evaluated by linear incision experimental models. The chloroform extract of *Echium italicum* L. was fractionated by successive chromatographic techniques. Wound healing activity of each fraction was investigated following the bioassay-guided fractionation procedures. The tissue samples of isolated compounds were examined histopathologically. The healing potential was comparatively assessed with a reference ointment Madecassol®, which contains 1% extract of Centella asiatica. Significant wound healing activity was observed from the ointment prepared with ethanol extract at 1% concentration. The ethanol root extract of E. italicum L showed a significant increase (37.38%) wound tensile strength in the incision wound model. Subfractions showed significant but reduced wound healing activity on in vivo wound models [60-61].

Equisetum arvense

The effect of *Equisetum arvense* 5% on wound healing in rabbits was investigated and compared to povidone iodine and sodium chloride. Skin wounds were created on their dorsal aspect. Postoperatively, the wound surfaces were macroscopically examined, the healing process and the rates of wound expansion, contraction and epithelization were examined. Biopsy specimens were collected on the 4, 7, 10 and 14th postoperative days to dedtermine neutrophil, macrophage infiltration, fibroblast and fibrosyctes. 5% Equisetum arvense caused wound contraction comparable to povidone iodine and sodium chloridein the 10th day of the treatment. Differences in wound contraction of *Equisetum arvense* 5% treated rabbits between postoperative 4th days and postoperative 14th days were significant but between 7th and 14th day was nonsignificant. However, in postoperative 4, 7, 10 and 14 days, the differences between the neutrophil, macrophage infiltration, fibroblast and fibrocytes were nonsignificant [62].

The effectiveness of topical application of *Equisetum arvense* ointment 3% in wound healing, reduction of inflammation and pain relief after episiotomy was studied in nulliparous mothers. A double-blind clinical trial was performed on 108 postpartum nulliparous mothers (54 women in horsetail group and 54 women in placebo group). About 5 ± 1 and 10 ± 1 days after the childbirth, the primary outcomes of episiotomy (wound healing and pain intensity) were assessed based on redness, edema, ecchymosis, discharge and approximation of the edges (REEDA) scale and a visual analogue scale (VAS). The number of used painkillers and the adverse events during the 10-day treatment period were recorded. The mean scores were significantly lower in the treated group than the control group. The adjusted pain score difference (MD) after 5 ± 1 and 10 ± 1 days was -2.3 (95% CI: -3.2 to -1.3) and 3.8 (95% CI: -4.7 to -3.0), respectively. The mean numbers of acetaminophen pills used in the control and treated group during the 10-day period of the study were 6.8 ± 4.4 and 11.6 ± 7.1, respectively (P < 0.001). Accordingly, 3% Equisetum arvense ointment promoted wound healing and relieved pain during the 10-day period after episiotomy [63].

The effectiveness of *Equisetum arvense* ointment was evaluated in dermal wound (15 mm x 15 mm) healing in rats. The first group did not receive treatment while the second group was treated with a 1:1 mixture of Vaseline and lanolin ointment. *Equisetum arvense* 5% and 10% ointments were used in the third and fourth groups. *Equisetum arvense* 5% and 10% groups and the Vaseline-lanolin group had a statistically significant higher wound closure ratio than the control group ($P < 0.05$). *Equisetum arvense* ointment groups had a 95.26% and 99.96% wound closure ratio ($P < 0.05$) and higher dermal and epidermal regeneration, angiogenesis, and granulation tissue thickness after 14 days as compared to the other groups ($P < 0.05$) [64-65].

Euphorbia hirta

The wound healing effect of *E. hirta* was investigated by in vitro/in vivo wound healing models using human dermal fibroblast cell line and Wistar rats. Wound contraction, hydroxyproline content and the protein expression of COL3A1, bFGF, Smad-2,-3,-4 and -7 were measured. The *E. hirta* methanol extract showed significant fibroblast proliferating activity (112% at 12.5 µg/ml) as compared to other extracts. In vivo study also supported the wound healing potential of methanol extract, as evidenced by faster wound contraction, higher hydroxyproline (4.240 mg/100 mg tissue) and improved histopathology of granulation tissue as compared to control groups and gentamicin sulfate-treated ones. Western blot also revealed a significantly altered expression of Smad-mediated proteins resulting in collagen production [66].

The wound healing effect of *Euphorbia hirta* ethanolic leaves was evaluated in excision wound model (cutting away 500 mm^2 of the skin on the anterio-dorsal side under anesthesia) in rats. The extract was formulated as an ointment (5% and 10% W/W). The wound contraction was observed at different time intervals. Both the concentrations of *Euphorbia hirta* leaf extracts showed significant ($P<0.001$) wound contraction in this wound model in rats [67-68].

Foeniculum vulgare

The wound healing action of aqueous extract of *Foeniculum vulgare* (2% and 7% ointment) was studied in rats using excision wound model. Vaseline was used as control while Mupirocin was used as standard. Post treatment the % wound contraction and wound area was measured on 4th, 8th, 12th and 16th day. the results revealed significant decrease in wound area and in % wound contraction was induced by ointment of aqueous extract of *Foeniculum vulgare*[69].

Fraxinus ornus

The skin-regenerating properties of the ethanolic bark extract and its main component esculin was investigated in male rats with standard oval wounds. The wounds were evenly coated ,once a day for 15 days, with propylene glycol (solvent), 14.2% extract solution or 3.45% esculin solution. Rats treated with the bark extract, exhibited a more intense epithelization of the wounds in comparison with the control groups in all stage of the investigation. A weaker regenerating effect was found in group treated with esculin[70-71].

***Gossypium* species**

The healing activity of *Gossypium herbaceum* leaves methanolic extract has been proved by using excision wound, incision wound and dead space wound models in rats. In incision and excision models, a significant decrease in period of epithelization and wound contraction was observed in all the treatment groups when compared to control. In the incision wound model, a significant increase in the breaking strength was observed. Granulation tissue formation significantly increased in all treated animals compare to control[72].

The wound healing activity of ethanol and ethyl ether fractions of leaves of *Gossypium herbaceum* was investigated by dexamethasone delayed wound healing model in rats. *Gossypium herbaceum* decreased glucose level against dexamethasone. In excision wound model wound contraction area was increased, the epithelization period and scar area were decreased with significantly increase in percentage of wound healing in *Gossypium herbaceum* treated groups. In incision mode, a combination of extract plus dexamethasone significantly increases the breaking strength. Hydroxyproline content significantly increased in the treated groups compare to dexamethasone group[73].

Hibiscus rosa-sinensis

The wound-healing activity of the ethanolic extract of the flowers of *Hibiscus rosa sinensis* (5 and 10% w/w) was studied in rats using three different models (excision, incision and dead space wound). The extract increased cellular proliferation and collagen synthesis at the wound site, as evidenced by increase in DNA, total protein and total collagen content of granulation tissues. The extract-treated wounds were found to heal much faster as indicated by improved rates of epithelialization and wound contraction. The extract of *H. rosa sinensis* significantly ($P<0.001$) increased the wound-breaking strength in the incision wound model compared to controls. The extract-treated wounds were found to epithelialize faster, and the rate of wound

contraction was significantly (P<0.001) increased as compared to control wounds. Wet and dry granulation tissue weights in a dead space wound model increased significantly (P<0.001)[74].

The efficacy and possible mechanism of the N-butyl alcohol extract of Hibiscus rosa-sinensis red flowers (NHRS) was investigated in wound healing using an excisional wound healing model in rats, different concentrations of NHRS, or recombinant bovine basic fibroblast growth factor (rbFGF), were applied twice daily for 9 days. Histopathology was assessed on day 9 using hematoxylin and eosin, Masson's trichrome staining, and immunohistochemistry for vascular endothelial growth factor (VEGF), transforming growth factor-β1 (TGF-β1) and CD68. Immunomodulation by NHRS was evaluated by a carbon clearance test in mice. NHRS accelerates wound repair via enhancing the macrophages activity, accelerating angiogenesis and collagen fiber deposition response mediated by VEGF and TGF-β1[75].

Healing enhancing effect of *Hibiscus rosa sinensis* was assessed by the rate of wound contraction, period of epithelialization, tensile strength (skin breaking strength), granulation tissue weight, and hydroxyproline content. Animals treated with the extract exhibited an 86% reduction in the wound area compared with controls, who exhibited a 75% reduction. The extract-treated animals were found to epithelize their wounds significantly faster than controls (P < .002) and have shown significantly higher skin-breaking strength than controls (P < .002). The dry and wet weight of granulation tissue and hydroxyproline content were also increased significantly when compared with controls[76].

Hibiscus sabdariffa

The wound healing activities of water in oil cream of the methanol extract of *Hibiscus sabdariffa* was evaluated in rats with superficial skin excision wounds. Creams containing *H. sabdariffa* extract showed significant (P<0.05) and concentration dependent wound healing activities. There was also evidence of synergism with creams containing a combination of gentamicin and *H. sabdariffa* extract [77].

Jasminum sambac

The ethanol stems extract of Jasminum sambac was evaluated for wound healing activity in the ointment dosage form in excision wound model in mice. The extract was tested for wound healing activity at two dose level (200 and 400 mg/kg bw) using dermal route. Total ethanol extract at dose level of 400mg/kg body weight had shown significant increase in wound contraction, hydroxyproline content and decreased epithelization period in excision wound model as compared to control group[78].

The aqueous and ethanol extracts of *Jasminum sambac* leaves were evaluated for its wound healing (200 and 400mg/kg bw, by dermal route), in excision wound model using albino mice. Aqueous extract had shown significant increase in wound contraction, hydroxyproline content and decreased epithelization period in excision wound model as compared to ethanol extract. The authors postulated that the enhanced wound healing activity of aqueous extract may be due to free radical scavenging action and antibacterial property of the phytoconstituents(tannins and flavonoids) identified in the extract[79].

The aqueous and ethanolic extracts of the leaves of *of Jasminum sambac*were incorporated in simple ointment base and screened for wound healing activity using (excision, incision and dead space wound models) in rats . The extracts possessed significant wound healing in all models[80-81].

Burns healing:

Aloe vera

Many studies showed that aloe hasten wound healing cause by burns, frostbite, electrical injuries, caustic chemicals and surgery[82-83].

Calendula officinalis

Effect of *Calendula officinalis* flower extract was investigated against experimentally induced thermal burns in rats. Burn injury was made on the shaven back of the rats under anesthesia and the animals were treated orally with different doses of the flower extract (20 mg, 100 mg and 200 mg/kg body weight). The animals treated with the extract showed significant improvement in healing when compared with the control untreated animals. The indicators of the wound healing such as collagen-hydroxyproline and hexosamine contents were significantly increased in the treated group indicating accelerated wound healing in the treated animals. The acute phase proteins-haptoglobin and orosomucoid which were increased due to burn injury were found to be decreased significantly in 200 mg/kg body weight extract treated animals. The antioxidant defense mechanism, which was decreased in the liver during burn injury, was found to be enhanced in treated animals. The lipid peroxidation was significantly lowered in the treated group when compared to control animals. Tissue damage marker enzymes (alkaline phosphatase, alanine and aspartate transaminases) were significantly lowered in the treated groups in a dose dependant manner. The histopathological analyses of skin tissue also gave the evidence of the increased healing potential of the extract after burn injury [84].

Crocus sativus

The efficacy of pollen of saffron extract cream was evaluated in the treatment of thermal induced burn wounds and to compare its results with silver sulfadiazine (SSD) in rats. Animals were divided into four groups and administrated a topical cream including control, base, saffron (20%) or SSD (1%) at 24 hour after a burn injury that was induced by hot water. Animal's weight, wound size, as well as skin histopathology were determined in different groups under topical treatments. On day 25, average size of wound was 5.5, 4, 0.9 and 4.1 cm^2 in control, base, saffron and SSD groups. The wound size of saffron group was significantly smaller than other groups. Histological comparison has shown that saffron significantly increased re-epithelialization in burn wounds, as compared to other cream-treated wounds [85].

Euphorbia hirta

The effect of whole *E. hirta* ethanol extract as 2% W/W cream was evaluated for burn wound healing activity in rats. The percentage reduction in original wound of *E. hirta* treated animals was showed significant burn wound healing activity [86-87].

Jasminum officinale

Ampucare is a topical oil-based preparation containing *Azadirachta indica, Berberis aristata, Curcuma longa, Glycyrrhiza glabra, Jasminum officinale, Pongamia pinnata,Rubia cordifolia, Terminalia chebula, Trichosanthes dioica, Symplocos racemosa, Ichnocarpus frutescens, Capsicum abbreviata, Nymphaea lotus* etc. Application of ampucare in second-degree burn showed burn healing effect with enhancement of antioxidant function It increased wound contraction,; decreased NO, decreased xanthine oxidase activity, increased protein level, increased vitamin C, reduced glutathione and decreased MDA in blood samples[88-91].

Effect on hair:

Adiantum capillus-veneris

The hair growth-promoting activity of a preparation of the *Adiantum capillus-veneris* was evaluated on albino mice using a testosterone-induced alopecia model. *Adiantum capillus-veneris* solution was applied topically to the back skin of animals and hair growth was evaluated by visual observation and histological study of several skin sections via various parameters as follicle density (number of follicles/mm) and anagen/telogen ratio. After 21 days, a patch of diffuse hair loss was seen in animals received testosterone while animals treated with *Adiantum capillus-veneris* showed less hair loss as compared to those treated with testosterone only. The follicular density observed in the *Adiantum capillus-veneris* -treated group was 1.92 ± 0.47, compared to 1.05 ± 0.21 in testosterone-group and 2.05 ± 0.49 (follicles/mm) in finasteride-treated animals. Anagen/telogen ratio was significantly affected by *Adiantum capillus-veneris* , which was 0.92 ± 0.06 as compared with 0.23 ± 0.03 and 1.12 ± 0.06 for testosterone and finasteride treated groups, respectively [93-93].

Allium sativum

The topical use of garlic gel in a double-blinded randomized controlled trial was significantly increase the therapeutic efficacy of topical betamethasone valerate in alopecia areata and it can be an effective adjunctive topical therapy for alopecia areata [94].

Carthamus tinctorius

It appeared that *Carthamus tinctorius* was sufficiently characterized for the maintenance of skin and hair when used as safflower seed oil 314 and 50 mg/day respectively [69]. The potential of hydroxysafflor yellow A-rich *C. tinctorius* extract (CTE) was examined on hair growth both *in vitro* and *in vivo*. The effect of CTE on cell proliferation and hair growth-associated gene expression in dermal papilla cells and keratinocytes (HaCaT) was determined. In addition, hair follicles from mouse neonates were isolated and cultured in media supplemented with CTE. Moreover, CTE was applied topically on the hair-shaved skin of female C57BL/6 mice, and the histological profile of the skin was investigated. *C. tinctorius* floret ethanolic extract promoted the proliferation of both dermal papilla cells and HaCaT and significantly stimulated hair growth-promoting genes, including vascular endothelial growth factor and keratinocyte growth factor. In contrast, CTE suppressed the expression of transforming growth factor-β1 that is the hair loss-related gene. Furthermore, CTE treatment resulted in a significant increase in the length of cultured hair follicles and stimulated the growth of hair with local effects in mice [95].

Cistanche tubulosa

Cistanche tubulosa extract was studied in double-blinded, placebo-controlled clinical trial, to investigate its efficacy in promoting hair health in patients with mild to moderate patterned hair loss. The density and diameter of hairs was compared with that in patients receiving a placebo at baseline, 8 and 16 weeks of the study. In order to determine the efficacy of treatment on dandruff and scalp inflammation,

investigator's visual assessment score and patient's subjective score were also performed. A statistically significant increase in the hair density and hair diameter of the test group was recorded after 16 weeks. There were also significant outcomes regarding the investigator's visual assessment and patient's subjective score of dandruff and scalp inflammation in the test group compared to those in control group. Based on the results of this clinical study, the authors conclude that *Cistanche tubulosa* extract *is a* promising substances for promoting health of the scalp and hair [96].

Citrullus colocynthis

Petroleum ether and ethanol extracts of *Citrullus colocynthis* were tested for their effect on hair growth in albino rats. The extracts incorporated into oleaginous ointment base were applied topically on shaved denuded skin of albino rats. The time required for initiation of hair growth as well as completion of hair growth cycle was recorded. Minoxidil 2% solution was applied topically and served as the standard. Hair growth initiation time was significantly reduced to half on treatment with the petroleum ether extracts compared with untreated control animals. The time required for complete hair growth was also considerably reduced. The treatment was successful in bringing a greater number of hair follicles (>70%) to anagenic phase than standard minoxidil (67%). The result of treatment with 2 and 5% petroleum ether extracts were comparable with the standard minoxidil [97-98].

Cyperus rotuntdus

The efficacy of topical *Cyperus rotundus* oil to decrease hair growth, was evaluated by an open-label pilot study. Eligible participants (n=65) with unwanted axillary hair were assigned randomly to 3 study groups: topical *Cyperus rotundus* oil (group 1), saline (group 2), and Alexandrite laser (group 3). Three methods were used to evaluate the results: hair counts, observations of independent professionals, and patient self-assessments. Overall results did not differ significantly between *Cyperus rotundus* oil and the Alexandrite laser ($p>0.05$). However, statistically significant differences were noted with respect to decrease of growth of white hair ($p<0.05$), favoring the oil. This finding was evident by all 3 methods (hair counts, observations of independent professionals, and patient self-assessments) of assessment. No side effects were detected [99-100].

Daucus carota

Animal studies were carried out by application of standardized Daucus *carota* extract in gel formulation to the shaved dorsal skin of albino rats, then histomorphometric analysis was employed to study induction of the hair follicle cycle. To determine the effect of extract on the telogen to anagen transition, the protein expression levels of β-catenin in hair follicles were determined by immunohistochemistry. The results showed that pet ether Daucus *carota* extract promoted hair growth by inducing the anagen phase. Specifically the histomorphometric analysis data indicates that topical application of the extract in gel form induced an earlier anagen phase and prolonged the mature anagen phase, in contrast to control and 1% minoxidil treated group. Results also revealed an increase in both the numbers and size of hair follicles of the extract treated group. Moreover, the immunehistochemical analysis revealed earlier induction of β-catenin in hair follicles of the extract-treated group, compared to the control group [101].

***Eucalyptus* species**

A long-term usage investigation of a scalp lotion containing Eucalyptus extract, was carried out to explore the change in physical properties of the hair fiber. Half-head or whole-head usage studies of a scalp lotion with Eucalyptus extract were carried out for the following groups: Japanese female, Japanese senior female, Japanese male, and Caucasian female panelists. The improvement in hair luster and bounce in the root part of the hair were recognized by the panelists after the long-term application of the scalp lotion with Eucalyptus extract. Measurement of hair gloss intensity and bending stress at the root suggests that this improvement is based on changes in these physical properties. The results indicated that the recognition of panelists is based on an actual change in the hair fiber properties. The efficacy of Eucalyptus extract is expressed regardless of race, age, or gender, since similar results were confirmed in all panelist groups. To study the mechanism, the elasticity (Young's modulus) of the new-growth part of the cortex in Eucalyptus extract-treated hair and placebo hair were evaluated by the nano-indentation method of atomic force microscopy (AFM). The results suggested that the Young's modulus of the new-growth part of the cortex in Eucalyptus extract treated-hair increases in comparison with placebo hair. The IR spectra of treated samples of hair show changes that appear to confirm a decrease in the alpha-helix structure and an increase in the beta-sheet structure [102].

Foeniculum vulgare

The response of idiopathic hirsutism to topical *Foeniculum vulgare* extract cream was evaluated clinically in a double blind study. 38 patients were treated with creams containing 1%, 2% of *Foeniculum vulgare* extract and placebo. Hair diameter and rate of growth were evaluated. The efficacy of treatment with the cream containing 2% *Foeniculum vulgare* was better than the cream containing 1% *Foeniculum vulgare* and these two were more potent than placebo. The mean values of hair diameter reduction was 7.8%, 18.3% and -0.5% for patients receiving the creams containing 1%, 2% and 0% (placebo) respectively[103].

The effect of fennel topical gel on mild to moderate idiopathic hirsutism was studied by randomized, double-blind, placebo-controlled clinical trial using forty four women with mild to moderate idiopathic hirsutism. The case group received fennel gel 3% and the control group received placebo. The effect of fennel gel 3% was defined as reduction of thickness of facial hair in micrometer by microscope in comparison with placebo. Measurements were performed at zero time and 24 weeks after treatment. Hair thickness was similar between the two groups before intervention. The hair thickness reduced from 97.9±31.5 to 75.6±26.7 micron in patients receiving fennel gel after 24 weeks ($P<0.001$). Four patients complained of itching (3 in case group) and 4 patients complained of irritation and itching (3 in case group). However, this difference was not statistically significant [104].

Glycyrrhiza glabra

Liquorice showed hair growth stimulatory activity. The hydro-alcoholic Comparison between liquorice extract and Minoxidil 2%, showed that, 2% concentration of liquorice hydro-alcoholic extract possessed better hair growth stimulatory activity than 2% Minoxidil [105].

***Gossypium* species**

Cotton honeydew extract is composed of a unique combination of oligosaccharides, including fructose, glucose, inositol, melezitose, saccharose, trehalose and trehalulose. Studies have shown that these oligosaccharides exhibit a protective effect. Furthermore, the effect of these oligosaccharides was studied in normal and damaged human hair. Both clinical and scanning electron microscopy (SEM) studies were performed. Standardized human hair samples were used to determine the effect of a rinse-off mask with 1% cotton honeydew extract on the ultrastructure of hair. In addition, hair samples were submitted to different aggressions, following various experimental protocols. SEM showed that, without extra aggression, the cuticle scales appeared to lie more smoothly in the hair in cotton honeydew extract-treated samples than in untreated samples. The extract-treated hair samples were also less prone to chipping. In a clinical study, 15 volunteers had half of their hair treated with a formula with 1% honeydew extract and the other half was left untreated as a control. Pictures and visual evaluation of the hair showed that the honeydew extract formula left the hair with a smoothness and this result was confirmed by SEM. In addition, mRNA studies on epidermal cells were confirmed the stimulating effect of honeydew extract on keratin synthesis[106].

Hibiscus rosa-sinensis

The effect of *Hibiscus rosa sinensis* (HRSF), *Calotropis gigantea* (CGF) and Polyherbal formulation. (HCF), a combination of both plants extract (petroleum ether leaf extracts were incorporated into hair cream base prepared by fusion method) was investigated in stimulating hair growth in stress induced alopecia animal model in comparison with Minoxidil . Thus on comparison HRSF, CGF, HCF and Minoxidil it has been observed that HRSF as well as HCF herbal formulation application showed better growth that the patch with minoxidil. The hair growth studies revealed that HRSF possessed excellent hair growth promoting activity by an enlargement of follicular size and a prolongation of the anagen phase. The hair growth activity was also observed in CGF but less in comparison to HRSF while the hair growth activity in animals treated a combination of both extracts was found to be significant when all the groups were compared statistically[107].

The petroleum ether extract of leaves and flowers of Hibiscus rosa-sinensis was evaluated for its effect on hair growth by in vivo and in vitro methods. In vivo, 1% extract of leaves and flowers in liquid paraffin was applied topically over the shaved skin of rats and assessed for 30 days. The length of hair and the different cyclic phases of hair follicles, like anagen and telogen phases, were determined at different time periods. In vitro, the hair follicles from rat neonates were isolated and cultured in DMEM supplemented with 0.01 mg/ml petroleum ether extract of leaves and flowers. The results revealed that the leaf extract exhibited more potency on hair growth when compared to flower extract[108].

The effect of ethanolic extract of Hibiscus rosa sinensis leaves was studied on androgenic alopecia. The animals treated with testosterone and vehicle become alopecic from the second week of treatment, while animals treated with finasteride and ethanolic extract of Hibiscus rosa sinensis did not become alopecic, the follicular morphology gave further evidence to hair growth stimulatory effects[109].

The ethanolic extract of H. rosa sinensis flower was evaluated as hair growth promote in female rats. Skin was denuded with hair removing cream, electronic shavers and hair clippers for ensuring complete removal of hair. Then 2% solutions of H. rosa sinensis flowers were applied on shaved denuded skin twice a day for thirty days. During this period they were observed visually for pattern of hair growth studies and after treatment period their skin biopiosis were taken for follicular density and cyclic phases of hair growth. On the basis of visual observation of animals and histopathology, ethanolic extract of H. rosasinensis flowers showed shorter hair and take more time for growth and favours telogenic stage of hair follicles as compared to control thus it showed hair growth retarding activity inspite of hair growth promoting one[110].

Anticancer:

Allium sativum

The application of chloroform extracts of garlic result in the complete resolution of cutaneous warts without recurrence after 3–4 months in a placebo-controlled trial [111].

Diallyl disulfide from garlic (*Allium sativum*) has been shown to have an antiproliferative effect on human tumor cells including those of skin. The consumption of garlic and related sulfur compounds has been reported to inhibits N-methyl-N-nitrosourea induced mammary cancer, dimethylhydrazine induced colon cancer , 4-(methylnitrosamino)-1-(3- pyridyl)-1-butanone induced lung cancer, 1,2-dimethylhydrazine induced hepatic cancer, 7,12-dimethyl benz[*a*]anthracene and benzo[*a*]pyrene-induced skin cancer and carcinogen- induced stomach cancers in experimental animals [112-117].

Garlic oil increased glutathione (GSH) peroxidase activity in isolated epidermal cells incubated in the presence or absence of the potent tumor promoter 12-O-tetradecanoylphorbol-13-acetate (TPA), and inhibited the sharp decline in the intracellular ratio of reduced (GSH)/oxidized (GSSG) glutathione caused by TPA. According to these findings, it was postulated that the inhibitory effects of garlic oil on skin tumor promotion may result from their enhancement of the natural GSH-dependent antioxidant protective system of the epidermal cells [118-119]**.**

Bauhinia variegata

The methanolic extract of stem bark of *B. variegate* (at a dose of 500 and 1000 mg/kg bw) exerted anticancer effects in skin papilloma model against 7, 12- dimethylbenz (a) anthracene and croton oil induced skin carcinogenesis in mice. It was effective in decreasing the rate of tumor incidence and the cumulative number of papillomas. Tumor yield and tumor burden were also found to be reduced. The depleted level of glutathione was restored in *B. variegata* bark extract treated groups [120].

Carthamus tinctorius

The mixture of erythro-alkane-6,8-diols from the flowers of *C. tinctorius* markedly suppressed the promoting effect of TPA (12-0-Tetradecanoylphorbol-13-acetate) on skin tumor formation in mice following initiation with 7,12-dimethylbenz [a]anthracene [121-122].

Chrozophora tinctoria

The inhibitory effect of *Chrozophora tinctoria* on mouse skin tumors was studied in vivo, tumor initiation was achieved by a single topical application of 7, 12-Dimethylbenze (a) anthracene (DMBA) (40 µg/100 µl acetane/mouse). After 7 days, tumor promotion was begun by twice-weekly topical application of Benzoyl peroxide (BPO) (20 mg/300 µl acetone/mouse) for a period of 32 weeks. Also before 4 hours of DMBA application , animals received a single topical dose of *Chrozophora tinctoria* extract (10 mg/gr carbopol gel/mouse). Results showed that there were higher yields of tumors in those animals receiving both DMBA and BPO. However, the *Chrozophora tinctoria* pretreated group showed complete inhibition of tumor incidence. The authors suggested that the antitumor effect of the plant was mediated by its scavenging of free radicals which play an important role in skin cancer [123-124].

Clerodendron inerme

The anticancer effects of ethanolic extract was investigated in 7,12- dimethylbenz(a) anthracene (DMBA) induced skin carcinogenesis in Swiss albino mice. Extract at a dose of 300 mg/kg significantly prevented the tumor formation as well as restored the status of glycoconjugates and red blood cell osmotic fragility in DMBA treated animals[125-126].

The chemopreventive and antilipidperoxidative effect of the ethanolic extract of *Clerodendron inerme* leaves were studied in 7,12- dimethylbenz(a) anthracene (DMBA) induced skin squamous cell carcinoma in mice. Oral administration of the ethanolic extract of *Clerodendron inerme* leaves (300 mg/ kg bw) for 25 weeks significantly prevented the tumor incidence, volume and burden of tumor. The ethanolic

extract of *Clerodendron inerme* leaves also showed potent antilipidperoxidative effect as well as enhanced the antioxidant defense mechanisms in DMBA painted mice[127].

Convolvulus arvensis

The cytotoxic effect of *Convolvulus arvensis* (methanolic extract) was evaluated against 2 stage skin carcinogenesis protocol, by tumor initiator, 7-12-dimethyl benz(a)antheracene (DMBA) and tumor promoter, croton oil in Swiss albino mice. Local application of the extract at 300 mg/kg/day inhibited the tumor incidence up to 20% in 16 weeks[128-129].

Coriandrum sativum

The protective effect of *Coriandrum sativum* (CS) against 2,4-dinitrochlorobenzene-induced CD-like skin lesions was studied in mice. CS, at doses of 0.5-1%, applied to the dorsal skin inhibited the development of CD-like skin lesions. Moreover, the Th2-mediated inflammatory cytokines, immunoglobulin E, tumor necrosis factor-α, interferon-γ, interleukin (IL)-1, IL-4, and IL-13, were significantly reduced. In addition, CS increased the levels of total glutathione and heme oxygenase-1 protein. Thus, CS inhibited the development of CD-like skin lesions in mice by regulating immune mediators and may be an effective alternative therapy for contact diseases [130].

Crocus sativus

Saffron treatments were given both before and after the induction of skin carcinogenesis. Standard histological examination of mice skin demonstrated that saffron ingestion inhibited the formation of skin papillomas and reduced their size. Saffron extract inhibited skin carcinoma due to the induction of cellular defense systems in mice [131].

Daucus carota

The effect of *Daucus carota* fraction, pentane/diethyl ether (50:50), on was investigated skin cancer cell motility and invasion. A pronounced decrease in cancer cell motility was observed. The treatment also led to a decrease in cancer cell invasion and an increased cell adhesion. Additionally, the *Daucus carota* fraction decreased the activation of the ρ-GTPases Rac and CDC42, a finding which may partially explain the decrease in cell motility [132].

The chemopreventive effects of oil extract from *Daucus carota* umbels was investigated on 7,12-dimethyl benz(a)anthracene (DMBA)-induced skin papilloma in mice. Topical 100% treatment delayed tumor appearance, and inhibited tumor incidence and yield by 40 and 89%, respectively. Topical 50% treatment inhibited tumor incidence and yield by 30 and 83%, respectively, whereas the 5% treatment inhibited tumor yield by 36%. Tumor volume was decreased by 99, 91, and 70% following topical treatments with 100, 50, and 5% oil, respectively. Intraperitoneal treatment inhibited tumor yield by 43%, and decreased tumor volume by 85%, whereas gavage treatment showed minimal effects[133].

Hibiscus rosa-sinensis

Hibiscus rosa sinensis extract possessed a protective effect against the tumour promotion stage of cancer development. The ameliorative potential of *Hibiscus rosa sinensis* extract was investigated in hyperproliferation and oxidative damage caused by benzoyl peroxide and ultraviolet radiations in mouse skin. Pretreatment with *H. rosa sinensis* extract (3.5 mg and 7 mg/ kg bw) partly restored the levels of cellular protective enzymes ($P<0.05$). Besides, malondialdehyde formation and hydrogen peroxide content ($P<0.05$) were statistically significantly reduced at both doses. The ornithine decarboxylase activity and thymidine incorporation in DNA were also reduced dose dependently ($P<0.05$) by the plant extract[135].

The role of gentisic acid in the chemopreventive activity of Hibiscus rosa sinensis extract was studied in 7,12-dimethyl benz(a)anthracene (DMBA)/croton oil-mediated carcinogenesis in mouse skin via 12-O-tetradecanoyl phorbol-13-acetate (TPA)-induced tumour promotion response and oxidative stress. Application of H. rosa sinensis extract 30 minutes prior to the application of croton oil twice weekly for 20 weeks caused significant reduction in the number of tumours per mouse and the percentage of tumour-bearing mice. The latency period for the appearance of the first tumour was delayed on H. rosa sinensis pretreatment. Pretreatment of H. rosa sinensis extract (3.5 mg and 7 mg/kg bw) and gentisic acid (2.0 microg and 4.0 microg/0.2 ml acetone per animal) restored the levels of GSH, and its metabolizing and antioxidant enzymes ($P<0.05$). There was also a statistically significant reduction in MDA formation and H_2O_2 content ($P<0.05$) at both doses. The authors postulated that gentisic acid has a role in the modulatory activity of H. rosa sinensis extract[136].

The methanol extracts of 56 plant parts from 47 medical and edible plants cultivated in Okinawa were tested for their proliferative effects on NB1RGB skin fibroblast cells. Methanol extracts of *Jasminum sambac* showed higher NB1RGB cell proliferation activity (>10%) than the control [137].

Juglans regia

The cytotoxic effects of Juglans regia extracts and juglone, a napthoquinone isolated from the chloroform extract of the root part of *Juglans regia* and used as starting material for the further synthesis of a novel series of triazolyl analogs, were studied against various human cancer cell lines. The different extracts of Juglans regia and the isolated compound (juglone) exhibited satisfactory cytotoxic activity against a panel of eight different human cancer cell lines including skin (A-431)[138].

Antibacterial and antifungal effects:

Allium sativum contains ajoene, which exerted antifungal activity. 34 patients treated topically with 0.4% ajoene cream once a day for tinea pedis, 79% were cleared within 7 days ,while others were cleared within 14 days. In a 3-month follow-up, all participants were free of fungus [139].

Alpinia galangal

It has been shown that essential oils from both fresh and dried rhizomes of galangal have antimicrobial activities against bacteria, fungi, yeast and parasite. Terpinen-4-ol, one of the monoterpenes in the essential oil from fresh galangal rhizomes, contains an antifungal activity against *Trichophyton mentagrophytes*. Acetoxychavicol acetate, a compound isolated from an n-pentane/diethyl ether-soluble extract of dried rhizomes, was active against some bacteria and many dermatophyte species [43-44]. *A. galanga* have antifungal activity against fungi resist the common antifungal products like amphotericin B and ketoconazole [45]. It exerted a concentration-dependent inhibition of the growth of zoonotic dermatophytes and the yeast-like *Candida albicans* [140-141].

Anchusa strigosa

The aqueous extract of *Anchusa strigosa* (15 mg ml−1 medium) produced antifungal activity , the means of percentage of mycelial inhibition against M. canis *T. mentagrophytes* and *T. violaceum* were l50.1±9.84 , 36.7±3.80 , and 71.7±1.91 respectively [142].

Asphodelus fistulosus

Asphodelus fistulosus showed antifungal activity against *Trichophyton violaceum* [143].

Daucus carota

The antimicrobial activity of the essential oil of *Daucus carota* subsp carota from Portugal was evaluated against several Gram positive and Gram negative bacteria, yeasts, dermatophytes, and *Aspergillus* strains. The results showed a significant activity towards Gram positive bacteria (MIC = 0.32–0.64 µl/ml), *Cryptococcus neoformans* (0.16 µl/ml), and dermatophytes (0.32–0.64 µl/ml). The inhibition of the germ tube formation and the effect of the oil on *Candida albicans* biofilms were also unveiled. The oil inhibited more than 50% of filamentation at concentrations as low as 0.04 µl/ml (MIC/128) and decreased both biofilm mass and cell viability [144].

Dodonaea viscosa

Antifungal activity of solvent extracts of leaves and shoot of *Dodonaea viscosa* was studied against fungi, *Aspergillus niger, Aspergillus flavus, Paecilomyces varioti, Microsporum gypseum, and Trichophyton rubrum* causing skin diseases. All crude extracts were found to be effective against the tested fungi. However chloroform has strong inhibitory activity against fungi as compared to ethanol, methanol, ethylacetate and aqueous extracts. The maximum inhibitory activity of the ethanol extract was observed against *P.variety, T. rubrum* and *M. gypseum* 81.82%, 80% and 73.34% respectively, while, it possessed moderate inhibitory activity against *A.flavus* 65.72% and minimum inhibitory activity against *A.niger* 62.5%. The maximum inhibitory activity of the ethyl acetate extract was observed against *T. rubrum, M. gypseum* and *P. varioti* 80%, 73.34 and 63.64% respectively, while it possessed moderate inhibitory activity against *A. flavus* 57.15 and minimum inhibitory activity against *A.niger* 50%. The maximum inhibory activity of the chloroform extract was recorded against *P.varioti T. rubrum* and *M. gypseum* 90.91%, 80% and 73.34% respectively, while it exerted moderate inhibitory activity against *A.flavus* 71.41% and minimum inhibitory activity against *A.niger* 50%. The maximum inhibitory activity of the methanol extract was observed against *P.varioti* and *T.rubrum* 81.82 and 80%, while, it possessed moderate inhibitory activity against *A.niger* and *A.flavus* 62.5% and 57.15% respectively and minimum inhibitory activity against *M.gypseum* 53.34%. The maximum inhibitory activity of

the aqueous extract was observed against *P.varioti*, *T.rubrum* and *A.niger* 81.82%, 80% and 75%, while, it exerted moderate inhibitory activity against *M.gypseum* 60% and minimum inhibitory activity against *A. flavus* 57.15% [145].
The fractions derived from hydroalcoholic extract of *Dodonaea viscosa* leaves was evaluated against *Candida albicans* (Cl. I. 4043). With the exception of aqueous fraction, all the fractions exhibited anticandidal activities (zone of inhibition ≥ 10 mm). The MIC of n-hexane fraction was 62.5 µg/ml [146].

Eryngium creticum
The antifungal effect *Eryngium creticum* aqueous extracts (15 micrograms/ml medium) was investigated against *M. canis, T. mentagrophytes* and *T. violaceum*. The percentage of mycelial inhibition was 12.4±4.26, 56.6±7.41 and 38.8±7.98% for the three fungi, respectively [147-148].

***Eucalyptus* species**
Methanolic leaf extracts of *Eucalyptus camaldulensis* were investigated for *in vitro* antifungal activities against *Microsporum canis, Microsporum gypseum, Tricophyton rubrum, Tricophyton schoenleinii, Tricophyton mentagrophytes* and *Epedermophyton floccosum*. *Eucalyptus camaldulensis* showed antifungal activity against all the tested dermatophytes with MIC values ranging from 0.4 to 1.6 mg/ml [149-150].

Euphorbia macroclada
The antibacterial and antifungal effects of *Euphorbia macroclada* methanol extracts of the flowering branches was studied against 6 bacteria, 2 dermatophyte species (*Trichophyton* sp., *Epidermophyton* sp.) and candida. Inhibition zone diameter (mm) of *Euphorbia macroclada* methanolic extracts of the flowering branches were: *Staphylococcus aureus*: 11±0.88, *Bacillus megaterium* :13±0.57, *Proteus vulgaris*: 11±0.57, *Klebsiella pneumoniae* : 9±0.33, *Escherichia coli*: 8.33±0.33, *Pseudomonas aeruginosa*: 13±0.57, *Candida albicans* : 12±0.33, *Candida glabrata* : 11±0.57, *Candida tropicalis* : 13±0.33, *Trichophyton sp*: 23±0.57, *Epidermophyton sp*.: 23±0.57 mm. The inhibition zone diameter (mm) *for Euphorbia macroclada* latex (500µg/disc) were *S. aureus:* 10±1.15, *B. megaterium:* 8.33±0.33, *P. vulgaris:* 9±0.57, *K. pneumonia:* 23±1.15, *E. coli:* 8.33±0.33, *P. aeruginosa:* 9±0.57, *C. albicans:* 21±1.15, *C. glabrata:* 15±1.15, *C. tropicalis:* 15±1.15, *Trichophyton* sp.: 15±1.15 and *Epidermophyton* sp.: 8±0.33. The MIC values of *Euphorbia macroclada* methanolic extract of the flowering branches were: *S. aureus*: 50, B *megaterium*: 25, *P. vulgaris*: 50, *K. pneumonia*: 100, *E. coli: 25, P. eruginosa*: 100, *C.albicans*: 2.5, *C. glabrata*: 50, *C. tropicalis* 100, *Trichophyton sp.*: 50 and *Epidermophyton sp.*: 50 µg. The percent of growth of resistant *Escherichia coli* when *Euphorbia macroclada* latex combined with antibiotics was, 80.8±6.4 when combined with chloramphenicol, 90.1 ±8.4%, with neomycin, 45.7±5.9% with doxycycline, 80.5±8.1% with clarithromycin, 72.5±7.6% with cephalexin and 99.7± 8.1% with nalidixic acid compared with blank (100%)[151-152].

Ficus religiosa
A combination of hot alcoholic extracts of *Ficus religiosa, Ficus infectoria* and *Piper* betel were found to be effective against resistant and sensitive strains (Gram negative resistant *Klebsiella* strains, sensitive *Klebsiella* strains, resistant *Enterobacter* strains, sensitive *Enterobacter* strains , resistant *Escherichia coli* strains, resistant *Pseudomonas* strains, sensitive *Pseudomonas aeruginosa* strains and tandard *Pseudomonas aeruginosa* ATCC 2862) and (Gram positive resistant *Staphylococcus* strains, sensitive *Staphylococcus* strains, resistant *Micrococcus* strain and standard *Staphylococcus aureus* ATCC 2901), isolated from skin and soft tissue infections. The combined extract was formulated in different ointment bases. The ointment showed bactericidal activity within 2 h against the resistant strain of *Pseudomonas* spp [153-155].

***Gossypium* species**
The antimicrobial activity of *Gossypium hirsutum* oils was investigated against *Escherichia coli, Trichophyton rubrum* and *Candida albicans* by agar well diffusion method. *Gossypium hirsutum* oils possessed antibacterial and antifungal activity with diameter of inhibition of 12.33, 10, 10.16 mm against *Escherichia coli, Trichophyton rubrum* and *Candida albicans* respectively at a concentration of 1 mg/ml[156].

Hedera helix
The antifungal activity of triterpenoid saponins was investigated in vitro by the agar dilution method. Monodesmosidic hederagenin derivatives exhibited a broad spectrum activity against yeast as well as dermatophyte species. alpha-Hederin was the most active compound, and *Candida glabrata* was the most susceptible strain[157]. The mode of anti Candidal action of α-hederin, was investigated by a haploinsufficiency screen. Saponin cytotoxicity is often attributed to membrane damage, however α-hederin

did not induce hypersensitivity with an aminophospholipid translocase deletion strain that is frequently hypersensitive to membrane damaging agents. The haploinsufficiency profile of α-hederin is most similar to that reported for drugs such as caspofungin that inhibit synthesis of the fungal cell wall[158].

Helianthus annuus

Sunflower oil is easily absorbed by the skin and provides deep nourishment and moisturizing. For these reasons, it is a popular ingredient in over-the-counter and homemade beauty products including lotions, creams and massage oils. It can retain moisture in the skin. It may also provide a protective barrier that resists infection in premature infants. Infants receiving a daily skin treatment of sunflower oil were 41% less likely to develop infections in the hospital[159-160].

Hyoscyamus niger

The antifungal activity of a crude steroidal glycoside extract, fractions of spirostanoles and individual glicosides was investigated *in vitro* against [Eight reference yeast strains: *Candida albicans* ATCC 90029, *Candida albicans* Y0109, *Candida albicans* 38248, *Candida tropicalis* IP 1275-81, *Candida parapsilosis* ATCC 22019, *Candida glabrata* ATCC 90030, *Candida kefyr* Y 0106, *Candida krusei* ATCC 6258 and *Candida lusitaniae* CBS 6936; Dermatophytes (one isolate of each species: *Trichophyton mentagrophytes*, *Trichophyton rubrum*, *Trichophyton soudanense*, *Microsporum canis*, *Microsporum gypseum*, *Epidermophyton fl occosum*, and *Cryptococcus neoformans*; filamentous fungi (one isolate of each species: *Aspergillus fumigatus*, *Aspergillus fl avus*,*Scopulariopsis brevicaulis*)]. *In vitro* spirostanol fraction and glycosides showed a broad spectrum of antifungal activity. Only slight differences in their fungicidal profi les were observed[161].

Jasminum sambac

The methanol extract and essential oil from the flowers and leaves of J. sambac were evaluated for antifungal activity against *Malassezia* sp. and non-*Malassezia* sp. isolated from human skin samples. The methanol extract of flowers and leaves of J. sambac and essential oil of flowers showed potential antifungal activity with inhibition zones of 11.10 ± 1.92, 12.90 ± 1.68, and 13.06 ± 0.26 mm, respectively, and minimum inhibitory concentration (MIC) values of 80mg/ml to 160mg/ml and 50%, respectively[162].

Antiviral effects:

Allium sativum:

Garlic extracts have been shown to have *in vitro* and *in vivo* antiviral activity against the human cytomegalovirus, herpes simplex virus type 1, herpes simplex virus type 2, vaccinia virus and vesicular stomatitis virus. The antiviral effect of diallyl thiosulfinate (allicin), allyl methyl thiosulfinate, methyl allyl thiosulfinate, ajoene, alliin, deoxyalliin, diallyl disulfide, and diallyl trisulfide was determined against selected viruses including, herpes simplex virus type 1, herpes simplex virus type 2, vaccinia virus and vesicular stomatitis virus. The order for virucidal activity generally was: ajoene > allicin > allyl methyl thiosulfinate > methyl allyl thiosulfinate. Ajoene was found in oil-macerates of garlic but not in fresh garlic extracts. Ajoene was found to block the integrin-dependent processes in a human immunodeficiency virus-infected cell system [163-166].

Calendula officinalis

A tincture of the flowers of *Calendula officinalis* suppressed the replication of herpes simplex *in vitro* [167].

Carthamus tinctorius

The antiviral activity of *Carthamus tinctorius* L. (CT) was examined against gamma herpes virus infection. The results showed that treatment with CT extracts disrupted KSHV latency in the viral-infected host cells. n- Hexane and ethanol fractions of CT extracts critically affected at least two stages of the KHSV life-cycle by abnormally inducing KSHV lytic reactivation and by severely preventing KSHV virion release from the viral host cells. In addition to the effects on KSHV itself, CT extract treatments induced cellular modifications by dysregulating cell-cycle and producing strong cytotoxicity [168].

Datura fastuosa

The antiviral activity of atropine was evaluated by plaque reduction test against *Herpes Simplex* virus. Atropine blocked the glycosylaton of viral proteins of *Herpes* virus and hence the production of new virions. Virions formed in the presence of atropine were non infectious [169-170].

Glycyrrhiza glabra

Glycyrrhiza glabra extracts and glycyrrhizic acid inhibited the replication of several viruses included Epstein-Barr virus, Herpes simplex virus, Hepatitis A virus, Hepatitis B virus,Hepatitis C virus, Human

cytomegalovirus, Human immunodeficiency virus, Influenza virus, SARS coronavirus and Varicella zoster virus[171-173].

Antiparasitic:

Betula alba

Root and stem flavonoids, terpenes and phenols present in ethanol, chloroform, and ethyl acetate soluble fraction; these were found to be the most active inhibiting fractions against all the tested strains of bacteria, fungi, and leishmania. While in leaves flavonoids, terpenes, and phenols were present in ethanol, chloroform, and n-butanol fractions which were the most active fractions against both types of microbes and protozoan (*Leishmania*) in in vitro study [174-175].

Allium sativum

In vivo and *in vitro* studies showed that garlic extract reduces footpad lesions in *Leishmania mexicana*-infected BALB/c mice by inducing IFN-gamma production from T cells as a Th1 immunomodulator. *In vitro*, extract decreased macrophage infection via induction of nitric oxide production [176].

The methanolic extract of *A. sativum* bulbs was screened for *in vitro* and *in vivo* antileishmanial activity against *Leishmania major* strain (NLB 145) and *L. donovani* strain (NLB 065). BALB/c mice and golden hamsters (*Mesocricetus auratus*) were used in *in vivo* studies of *L. major* and *L. donovani*. The extract showed IC50 values of 34.22 µg/ml and 37.41 µg/ml against *L. major* and *L. donovani* promastigotes respectively, compared to 1.74 µg/ml against *L. major* and 1.18 µg/ml against *L. donovani* for Amphotericin B. The multiplication indices for *L. major* and *L. donovani* amastigotes in macrophages treated with 100 µg/ml of the extract were significantly decreased[177-179].

Bryophyllum calycinum

The antileishmanial effect of the plant extracts and its flavonoids components was evaluated in *vivo* in murine model of cutaneous leishmaniasis. Quercetin 3- O-α-L-arabinopyranosyl, α-L-rhamnopyranoside, quercetin 3-O-α-L- rhamno pyranoside and free quercetin were able to control the lesion growth caused by *Leishmania* and significantly reduce the parasite load. These flavonoids were as effective as the crude aqueous extract which indicated that the antileishmanial effect could be attributed to flavonoids [180-181].

Cordia myxa

The anti-leishmanial activity of the mucilage extract of *Cordia myxa* was examined against promastigotes of *L. infantum* (MCAN/IR/96/LON49) and *L. major* (MRHO/IR/75/ER) (1×106 cells/ ml). They were seeded in a 96-well microtiter plate, in the presence of the serial concentrations (0, 0.61, 1.22, 2.44, 4.88, 9.75, 19.5, 39, 78, and 156 mg/ ml w/v) of the extract and then incubated at 24°C, for 72 hours. Antileishmanial activity was assayed by light microscopy and (3-(4,5-dimethylthiazol-2-yl)-2,5 diphenyl tetrazolium bromide) MTT method. The concentration inhibiting parasite growth by 50% (IC50value) was calculated with a sigmoid dose-response curve. Mucilage extract of *Cordia myxa* was active against promastigotes form of *L. major* and *L.infantum*, with an IC50 of 26 ± 2.2 mg/ml and an IC50 of 35 ± 2.2 mg/ml, respectively. The survival percentage of *L. major* and *L. infantum* promastigotes after 72 hours treatment appeared concentration dependent. Percentage of survival *Leishmania major* after 72 hours reached 17.68% in a concentration of 156 mg/ml, while the percentage of survival of *L. infantum* promastigotes after 72 hours reached 16.68% in a concentration of 156 mg/ml [182-183].

Gossypium hirsutum

The anti-leishmanial activity of methanolic extracts of *Gossypium hirsutum* was studied on *Leishmania major* promastigotes by colorimetric assay in comparison to a trivalent antimony compound (tartar emetic). The plant extracts and tartar emetic inhibited the growth of promastigote stage of *L.major* after 72 hours of incubation. Tartar emetic as positive control gave a 50% inhibitory concentration (IC_{50}) of 4.7µg/ml, while the IC_{50} values of G. hirsutum was 3.6 µg/ml[184-185].

Hedera helix

Saponins of ivy, *Hedera helix* possessed antileishmanial activity in vitro on promastigote and amastigote forms of *Leishmania infantum* and *Leishmania tropica*. Monodesmosides were found to be as effective on promastigote forms as the reference compound (pentamidine). Against amastigote forms only hederagenin exhibited a significant activity which was equivalent to that of the reference compound (N-methylglucamine antimonate)[186]. The in vivo activity of an alcoholic extract of Hedera helix (20% and 70% alcoholic extract) was studied in experimental ulcer of zoonotic cutaneous leishmaniasis (CL) in Balb/c mice. The results revealed that the main lesion size did not decrease significantly, and the small lesions did not

completely disappear after treatment by H. helix alcoholic extract. Amastigotes counts (mean ± SD) of the skin lesions decreased in placebo control and 20% concentration groups, but in negative control and 70% concentration groups the number of parasites did not reduce[187].

Juglans regia

The effects of topical application of the ointment-based extract (2 and 4% of 50% ethanol extract) of *Juglans regia* was studied on *Leishmania major* (MRHO/ IR/75/ ER) induced infection in mice. The results showed significant post-treatment decrease in the lesion size and parasite count in infected animals, compared to control groups[188].

Treatment of psoriasis:

Allium sativum

The activation of nuclear transcription factor kappaB which linked with psoriasis. This transcription factor can be interrupted by diallyl sulfide, S-allylmercaptocysteine and ajoene [189].

Aloe vera

Aloe vera was recently found to be a potential treatment for psoriasis. In a double-blind placebo-controlled study, 60 patients with slight to moderate plaque psoriasis were treated topically with either 0.5% hydrophilic aloe cream or placebo. The aloe treated group showed statistically significant improvement (83.3%) compared with the placebo group (6.6%). There were no adverse effects reported in the treatment group [190-191].

Ammi majus

Numerous studies have assessed the efficacy of Fructus *Ammi majus* andxanthotoxin for the treatment of vitiligo, psoriasis, and hypopigmentation tinea versicolor [192-199]. Xanthotoxin with exposure to either UV-A or UV-B radiation for the treatment of plaque psoriasis in 100 patients appeared effective in reducing the number of plaques [200]. Oral administration of 0.6 mg/kg bw of xanthotoxin with two UV-A radiation dosage regimens was used for treatment of patients with moderate–severe chronic plaque psoriasis. 42% of patients were clear 1 year after treatment and the treatment regimens were well tolerated [201].

Many other similar results were obtained in assessment of *Ammi majus* and its furanocoumarins in the treatment of psoriasis, vitiligo and tinea versicolor by many authors [193, 198, 202-204].

Bidens tripartita

Clinically, 70% ethanol extract of the aerial parts of the plant and an ointment containing 2.5% of the extract were used by 53 patients with psoriasis. After one week of oral administration of the extract (20 drops three times daily) with application of the ointment to the affected areas of the skin once a day, desquamation of the skin was decreased, and a decoloration of the psoriatic plaques was observed. 29 of the patients were clinically recovered, 22 patients were clinically improved and failure of the therapy was recorded in 2 patients [205-206].

The effectiveness of capsaicin was studied in the treatment of psoriasis. In vitro, capsaicin was found to inhibit phorbol ester-induced activation of transcription factors NF-κB and AP-1 [207].

In 44 patients with moderate and severe psoriasis, 0.025% capsaicin cream showed a significant decrease in scaling and erythema during a 6-week [208].

However, a double-blind study of 197 patients with psoriasis treated with the capsaicin cream four times daily for 6 weeks showed significant decrease in scaling, thickness, erythema, and pruritus [209].

Capsicum annuum* and *Capsicum frutescens

The effectiveness of capsaicin was studied in the treatment of psoriasis. In vitro, capsaicin was found to inhibit phorbol ester-induced activation of transcription factors NF-κB and AP-1 [210].

Treatment of vitiligo:

Ammi majus

Numerous studies have assessed the efficacy of Fructus *Ammi majus* andxanthotoxin for the treatment of vitiligo, psoriasis, and hypopigmentation tinea versicolor [192-199].

Experimentation with *Ammi majus* extracts was started in Egypt by El Mofti [29-30]. This followed by the work of Sidi and Bourgeois who used *Ammi majus* Linn, in six patients with vitiligo, five men and one woman. Their ages were from 30 to 50 years. *Ammi majus* Linn was used (a) by oral administration, (b) by local topical application at the affected sites followed by sun or ultraviolet lamp exposure, or, (c) by a combination of (a) and (b). Three of patients were subjected to the combined treatment, two only to topical treatment and one to

treatment by mouth for 5 months, and then to the combined treatment. The repigmentation appeared in all patients as pigmented minute macules with hair follicles in their center. These macules were distributed over the leukodermic plaques and increased progressively in size until they joined, forming larger islands. This was particularly distinct in the lesions on the trunk and on the extremities. On the face the repigmentation developed more rapidly and appeared to be progressing more from the periphery towards the center [211].

Many clinical trials were carried out to investigate the efficacy of *Ammi majus* in vitiligo, Patient with leukodermis took oral *Ammi majus* powderd fruits with exposing the affected patches to direct sunlight for 1 hour developed symptoms of itching, redness, oedema, vesiculation and oozing in the leukodermic patches. Within few days , the affected skin gradually started to display deep brown pigmentation [212].

In two small group of patients (eight patients each) with leukoderma treated with oral(0.05 g of *Ammi majus* three time daily) or liniment 1 g/100 ml, applied to the skin, with daily exposure of leukodermic areas to the sun for 0.5 hour or to UV light for 2 minutes, gradually increasing to 10 minutes , the leukodermic skin areas were inflamed and vesiculated, and the leukodermic areas began to show normal pigmentation [193].

However *Ammi majus* and its furanocoumarins constituents showed good results in many other clinical studies , 70% of the patients treated with an oral dose of 0.6 mg/kg bw of xanthotoxin 2 hours before exposure to sunlight three times per week with calcipotriol ointment in a randomized double-blind study, showed significant improvement [213].

Xanthotoxin with exposure to either UV-A or UV-B radiation for the treatment of plaque psoriasis in 100 patients appeared effective in reducing the number of plaques [200]. Oral administration of 0.6 mg/kg bw of xanthotoxin with two UV-A radiation dosage regimens was used for treatment of patients with moderate–severe chronic plaque psoriasis. 42% of patients were clear 1 year after treatment and the treatment regimens were well tolerated [201].

Many other similar results were obtained in assessment of *Ammi majus* and its furanocoumarins in the treatment of psoriasis, vitiligo and tinea versicolor by many authors [193, 198, 202-204]**.**

Ammi visnaga

A double-blind, placebo-controlled study of 60 people indicated that the combination of oral khellin (which is the main constituent of *Ammi visnaga*) and natural sun exposure caused repigmentation in 76.6% of the treatment group, in comparison, no improvement was seen in the control group receiving sunlight plus placebo [42].

A subsequent placebo-controlled study of 36 patients of vitiligo, showed that a topical khellin gel plus UVA caused repigmentation in 86.1% of the treated cases, as opposed to 66.6% in the placebo group [214].

Dalbergia sissoo

The cytotoxicity and *in-vitro* melanogenic activity on bark of *Dalbergia sissoo* were studied . The various successive bark extracts have been individually evaluated for trials of spontaneous melanin content, and cell viability by the MTT assay in murine B16F10 melanoma cells in-vitro. Based on the percentage of cell viability assay, graded concentration of extracts were taken for in vitro melanogenic activity. The result indicated that ethyl acetate extract of bark of *Dalbergia sissoo* was non-toxic and increased melanin activity as compared to hexane and ethanol extracts. The authors concluded that the bark of *Dalbergia sissoo* stimulates B16F10 melanogenesis at very low concentrations which support the folk medicinal use of *Dalbergia sissoo* on the treatment of hypopigmentation diseases, such as vitiligo [215-216].

Depigmentation and skin lightening:

Bellis perennis

Bellis perennis was used as skin lightening drug (Belides TM , *Bellis perennis* flower extract). It affected the metabolic pathways involved in melanin synthesis. It inhibited tyrosinase, transcriptional control of tyrosinase expression, reduced pro-melanogenic mediators endothelin, and α MSH (melanin stimulating hormone), as well as reducing melanosome transfere keratinocyte [217].

Glycyrrhiza glabra

The extract of liquorice is reported to be an effective pigment lightening agent. Glabridin, in the hydrophobic fraction of liquorice extract inhibited tyrosinase activity in cultured B16 murine melanoma cells. Glabridin , licochalcone A and isoliquiritin were inhibited tyrosinase activity. *In vitro* tyrosinase enzyme inhibition studies has showed that 21.2 µg/ml of methanolic extract of liquorice caused 50% tyrosinase enzyme inhibition. Due to good tyrosinase inhibition activity, liquorice extract can be used to formulate cosmetic formulations with depigmenting activity. Ethanolic extract of *Glycyrrhiza glabra* is reported to show improvement in the viscoelastic and hydration properties of the skin[218-220].

A double blind placebo controlled study was carried out on one hundred female volunteers suffering from melasma (93 completed the study). Half of the females were used 2.5% of G. glabra extract cream and the other half were used placebo for 28 days. Comparison between the active treated cream and placebo on week interval indicated anon significant improvement for the first week of the treatment course (P=0.18). However, there was a significant difference in the improvement rate between the two treatment groups for week 2 (P=0.009), week 3 (P=0.005) and week 4 (P=0.001)[221].

Erigeron canadensis

The effects of Erigeron canadensis extract were investigated on melanogenesis and cell toxicity in cultured B16F10 mouse melanoma cells. E. canadensis extract down regulated melanin synthesis effectively at a non-toxic concentration. Its extract was fractionated into five fractions. One of the fractions showed melanin inhibition by 48.0% at 100 mg/ml which was 2.5 times more efficient than the depigmenting effect of commercial arbutin (17.5%) and also did not show cell toxicity. The in vitro and cellular tyrosinase activity, antioxidant activity, and protein level of the main melanogenic enzymes, such as tyrosinase, TRP-1 and TRP-2 were evaluated to elucidate the depigmenting mechanism of this fraction. The fraction inhibited melanin synthesis in B16F10 melanoma cells by decreasing protein levels of melanogenic enzymes, especially tyrosinase [222].

Photoprotective effects:

Calendula officinalis

The photoprotective effect of the topical formulations containing marigold extract (ME) (*Calendula officinalis* extract) was studied in ultraviolet (UV) B irradiation-induced skin damage. The physical and functional stabilities, as well as the skin penetration capacity, of the different topical formulations were evaluated. In addition, the *in vivo* capacity to prevent/treat the UVB irradiation-induced skin damage in hairless mice and skin penetration capacity of the formulation was investigated. All of the formulations were physically and functionally stable. The gel formulation was the most effective for the topical delivery of ME, which was detected as 0.21 μg/cm2 of narcissin and as 0.07 μg/cm2 of the rutin in the viable epidermis. This formulation was able to maintain glutathione reduced levels close to those of nonirradiated animals, but did not affect the gelatinase-9 and myeloperoxidase activities which increased by exposure to UVB irradiation. In addition, gel formulation reduced the histological skin changes induced by UVB irradiation that appear as modifications of collagen fibrils [223].

The *in vivo* protective effect of *Calendula officinalis* extract against UVB-induced oxidative stress in the skin of hairless mice was evaluated by determining reduced glutathione (GSH) levels and monitoring the secretion/activity of metalloproteinases. An oral treatment of hairless mice with 150 and 300 mg/kg of *Calendula officinalis* maintained GSH levels close to non-irradiated control mice. In addition, this extract affected the activity/secretion of matrix metalloproteinases 2 and 9 (MMP-2 and -9) stimulated by exposure to UVB irradiation [224].

Capparis spinosa

When *Capparis spinosa* applied topically it afforded significant *in vivo* protection against UVB light-induced skin erythema in healthy human volunteers [225].

Cassia occidentalis

The sun protection factor (SPF) for the flowers of *Cassia occidentalis* was studied. On comparison it was observed that *C. occidentalis* had high SPF value with antioxidant and antibacterial property. The results indicated that *Cassia occidentalis* flowers can be used for UV radiation hazards [226-227].

Coriandrum sativum

Coriandrum sativum ethanol extract (CSE) showed a protective effects against UVB-induced skin photoaging in normal human dermal fibroblasts (NHDF) *in vitro* and in the skin of hairless mice *in vivo*. The cellular levels of procollagen type I and MMP-1 were determined using ELISA in NHDF cells after UVB irradiation. NHDF cells that were treated with CSE after UVB irradiation exhibited higher procollagen type I production and lower levels of MMP-1 than untreated cells. The activity of transcription factor activator protein-1 (AP-1) was also inhibited by CSE treatment. CSE-treated mice had thinner epidermal layers and denser dermal collagen fibers than untreated mice. On a molecular level, it was further confirmed that CSE-treated mice had lower MMP-1 levels and higher procollagen type I levels than untreated mice [228].

Treatment of Acne:

Calamintha graveolens

The essential oils were frequently used in aromatherapy, topical creams, homeopathic natural medicine, and food products. It alleviated acne symptoms systemically when taken orally [229].

Citrus limon

The antibacterial activity of *Citrus limon* was studied against Acne vulgaris. *Citrus limon* juice was used at different concentrations of (20%, 40%, 60%, 80% and 100%) on *Propioni bacterium acne*. The *Citrus limon* juice was found to be effective at all concentrations used[230-231].

Colchicum candidum

Many of dermatological diseases were treated with colchicines including erythema nodosum leprosum, pyoderma gangrenosum, severe cystic acne, calcinosis cutis, keloids, sarcoid, condyloma acuminata, fibromatosis, relapsing polychondritis, primary anetoderma, subcorneal pustular dermatosis, erythema nodosum, scleredema, and actinic keratosis[232-233].

Cuminum cyminum

The volatile oil of *Cuminum cyminum* was active against *Staphylococcus epidermidis, S. aureus, S. haemolyticus* and *Propionibacterium acnes*[234-235].

Treatment of eczema:

Calotropis procera

Topical preparation of *C. procera* was used for the treatment of eczema in 94 patients. The trials were conducted for nine months. The result was found encouraging, complete cure of all the signs and symptoms have been noted in 14 (14.89%) patients, excellent response was noted in 24 (25.53%) patients, good response in 33 (35.10%) patients, fair response in 10 (10.63%) patients. Two (2.12%) patients showed poor response to the treatment and 2 (2.12%) patients exhibited worsened condition [236].

Fumaria parviflora

In a randomized double-blind, placebo-controlled study, 44 patients with hand eczema were randomly assigned to apply 4% cream of *Fumaria parviflora* or vehicle cream to hand twice daily for 4 weeks. The reduction of eczema area and severity index score before and two weeks after therapy was statistically significant between vehicles treated and 4% cream *Fumaria parviflora* treated patients. Only one patient showed side effect [erythema and population] [237-238].

Avena sativa

Oatmeal preparations were effective on a variety of dermatologic inflammatory diseases such as pruritus, atopic dermatitis, acneiform eruptions, and viral infections. Additionally, oatmeal plays a role in cosmetics preparations and skin protection against ultraviolet rays [(35)]. The dried seeds were used to make a decoction to relieve the symptoms of eczema, the soothing emollient activity of the seeds decreased itching and nourished the skin. Oat colloidal extract containing avenanthramides has also proved to have antihistamine and anti-irritation activity[239-242].

Antiaging effects:

Coriandrum sativum

The protective effect of a standardized coriander (CS) leaf extract was studied against oxidative stress in human HaCaT keratinocytes. CS significantly and dose-dependently protected cells against reduced cell viability caused by H_2O_2-induced damage, as assessed by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay. Other assays demonstrated that CS protected HaCaT cells by increasing the levels of glutathione and activities of oxidative defense enzymes, such as superoxide dismutase and catalase. Moreover, it increased the expression of activated Nrf2, which plays a crucial role in protecting skin cells against oxidative stress [243-244].

Iris pallida

Sweet iris acts on consequences of natural ageing at the conjunctive level of the dermis and the upper layer of the epidermis, at the level of the dermis, the sweet iris stimulates the synthesis of constituents of the extra-cell matrix - collagens, glycosaminoglycans, elastin and proteoglycans - while limiting the action of the enzyme that destroys them. In the same time, it helps to regenerate the epidermis in a well-balanced way by increasing the production and the differentiation of the cells of the epidermis, that slows down with ageing. Skin layers can get back their density and their global balance, which limit the creation of wrinkles. Anti-wrinkle effect of sweet iris was evaluated in women after 28 days of treatment (face) : it decrease of the total surface by 24%, decrease of the number of wrinkles by 19% and decrease of the length of wrinkles by 26%. 80% of women declared that their wrinkles seem to have decreased[245].

***Kochia scoparia* (*Bassia scoparia*)**

The antiaging effect of a mixture of extracts of Kochia scoparia and Rosa multiflora was studied in photoaging skin. Eighteen-week-old hairless mice were irradiated with UVA 14 J/cm2 and UVB 40 mJ/cm2 three times a week for 8 weeks. A mixture of extracts of Kochia scoparia and Rosa multiflora (KR) was topically applied on the dorsal skin of photoaging mice twice a day for 8 weeks. Tesaglitazar, a known PPAR α/γ agonist, and vehicle (propylene glycol:ethanol = 7:3, v/v) were applied as positive and negative controls, respectively. Dermal effects (including dermal thickness, collagen density, dermal expression of procollagen 1 and collagenase 13) and epidermal effects (including skin barrier function, epidermal proliferation, epidermal differentiation, and epidermal cytokines) were measured and compared. In photoaging murine skin, KR resulted in a significant recovery of dermal thickness as well as dermal fibroblasts, although it did not change dermal collagen density. KR increased the expression of dermal transforming growth factor (TGF)-β. The dermal effects of KR could be attributed to an increase in procollagen 1 expression, induced by TGF-β, and a decrease in MMP-13 expression. KR did not affect basal transepidermal water loss or stratum corneum integrity, but did decrease stratum corneum hydration. It also did not affect epidermal proliferation or epidermal differentiation. KR also decreased the expression of epidermal interleukin (IL)-1α[246-247].

II. CONCLUSION:

Several medicinal plants possessed a wide range of dermatological effects included antimicrobial, antiparasitic, anticancer, hair growth-promoting activity, for the treatment of eczema, acne, vitiligo and psoriasis, wound and burn healing, as skin lightening and skin protection therapy and to slow down skin ageing. The current review discussed the dermatological effects of medicinal plants as promising future drugs because of safety and effectiveness.

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