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Review Article

Integrative Dermatology – The Use of Herbals and Nutritional Supplements to Treat Dermatological Conditions

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Abstract

From humble beginnings at the dawn of time to it's advanced and successful status today, this essay traces the history of natural medicine and the development of integrated dermatology to what it is today. Some of the most well-known natural (international and Australian) products with an application in dermatology are discussed. The history and functions of the Psoriasis Eczema Clinic and the products developed by its founder, Prof. Michael Tirant, are explained.

Introduction

Integrative Dermatology is a relatively new term coined to describe treatment therapy that combines Complementary Medicine with Dermatology in the treatment of dermatological conditions. It was first explored in Fitzpatrick's Dermatology in General Medicine, Chapter 241 - Complementary and Alternative Medicine in Dermatology, published in 2007. The authors stated that "Complementary and Alternative medicine (CAM) in dermatology encompasses a wide variety of methods of diagnosis and treatment that either supplement or substitute for conventional dermatologic practice, drawing on an expanded knowledge base that includes CAM, conventional practice, and the latest research findings. Its diagnostic and therapeutic choices are made by combining these three knowledge bases, in what might also be termed integrative dermatology" [1].

In the late 70's and early 80's, the main treatment options for dermatological conditions were exclusively in the domain of mainstream or conventional medicine. However, in some western countries, Complementary Alternative Medicine (CAM) was becoming more popular. As patients began to seek alternative treatment approaches using natural therapies to treat their skin conditions, CAM practitioners, including naturopaths, began to experiment with western herbal medicine and traditional Chinese medicine to meet the needs of their patients. Naturopaths tended to rely heavily on anecdotal and traditional treatments from historical

data rather than on scientific research results.

History of Mainstream Medicine/Allopathic Medicine for Dermatological Conditions

Mainstream medicine, although effective, mainly focused on providing symptomatic relief using topicals and/ or systemic, either as orals or injectables. Corticosteroids were first introduced in the treatment of psoriasis in 1952 with the topical application of hydrocortisone. Later, the steroid molecule was fluoridated which allowed more potent steroids like fluocinolone acetonide, betamethasone valerate and clobestadol propionate to be developed. These were then enhanced with occlusive dressings or by using combination therapies with salicylic acid and tars [5].

The 50's also saw the introduction of folate inhibitors like methotrexate, in both topical and as systemic preparations. In the 70's, Retinoids, analogues of Vitamin A, began to be used, especially for erythrodermic and pustular psoriasis, again as topical and systemic, with the first clinical trial on Isotretinoin undertaken in 1972. Later, other second-generation Vitamin A analogues, Etretinate (Retinoic Acid) and Acitretin were introduced as either topical and/or systemic. In the mid 80's analogues of Vitamin D (Calciprotriol) was found to also be of benefit in the topical treatment of psoriasis and by the mid-90s oral calcitriol (Vitamin D) became available [5][6][7].

Phototherapy was and is still one of the most common treatment options for psoriasis, with narrowband UVB (nbUVB) or psoralen ultraviolet A (PUVA) the most widely used applications. In the 50's, Dr John Ingram developed a treatment regimen using ultraviolet B (UVB) radiation in conjunction with coal tar and anthralin paste, and by the 70's, broadband UVB was found to be effective in clearing mild forms of psoriasis, whilst ultraviolet A (UVA) irradiation in combination with either oral or topical application of psoralen, was also being used. By the 80's narrowband UVB (nbUVB) was found to be effective in treating psoriasis [8].

With the advent of biologics to treat autoimmune diseases such as Rheumatoid Arthritis, researchers experimented during the 90's in the treatments of various systemic and cutaneous diseases. Biologics are protein molecules produced by recombinant DNA technology, which target the specific sites in the immune - pathogenesis pathway of the diseases by blocking these pathways. Because of the specific action on the immune system, biologics are considered to have fewer side effects compared to the traditional immune - suppressants. However, the use of biologics is still limited because of the unknown long-term safety profile and various aspects of the biologics [9].

History of Complementary Alternative Medicine (CAM) and CAM Therapies for Dermatological conditions

Complementary Alternative Medicine (CAM) is mainly focused on treating the human body as a whole in the hope that the dermatological condition would benefit from their treatment(s). CAM includes naturopathic compounded creams using herbal ingredients, herbal systems and nutritional supplementation and “detox” diets.

The history of CAM and the treatment of dermatological conditions are founded on the use of specific herbs solely developed based on locally available plants and through trade in ethnobotanical remedies. Various schools of herbal use developed regionally in Europe,

the Middle East, Africa, India, China, Japan, Australia, and the Americas. The best-known systems still in use today are the Ayurvedic herbs originated from India, herbal treatments developed as part of traditional Chinese medicine (TCM) in China, and Western Herbal Medicine developed in the United States and based on European and Native American traditions and later influenced by TCM [10].

Unlike the developing countries where traditional medicine remains entrenched in the treatment of various conditions including skin conditions, Europe and the United States saw a steady decrease during the 1900's in the use of herbal treatments and the number of herbalists, as purified extracts and synthetic chemical drugs became available. However, from the 70's onwards there has been a steady resurgence in the use of herbal treatments and the number of visits to CAM practitioners. The causes for this are varied including:- the increase in the identification of serious side effects of chemical drugs, the increased cost of mainstream medications, the lack of long-term efficacy of mainstream medication and a general desire to return to nature, natural remedies and an alteration to diet to include organic produce. Thus herbal remedies, including those for skin conditions, are continually gaining greater popularity among patients and to a lesser degree greater tolerance and/ or acceptance among General Practitioners [10].

In the United States, the number of visits to CAM practitioners has grown rapidly, estimated to have increased from 427 million in 1990 to 629 million in 1997. This 1997 figure exceeded the number of

visits Americans made to all primary care physicians in the United States during that same year. Furthermore, it is estimated that between 50% and 75% of the US population is using some form of CAM at a given time [11].

In the European Union, there are approximately 150,000 dual-trained doctors, meaning trained in conventional medicine and a particular CAM modality. In addition to these dually trained doctors, there are in the order of 180,000 non-doctor CAM practitioners. However, the prevalence rates of the main therapies in use are much harder to define, as statistical records are basic at best and therapies monitored and reporting methods differ from country to country. As an example, for Herbal Medicine (31 studies), the prevalence rates varied from 5.9 - 48.3% of the population studies. However, herbal medicine was not well defined (it may have been included in naturopathy, folk medicine or traditional Chinese medicine) and different categories including medical herbalism, herbal remedies, herbal teas and Phytotherapy [12].

Notwithstanding the number of alternate therapies that are included under the banner of CAM, for this review, the following will be considered: TCM, Ayurveda and Western Herbal Medicine and Naturopathy.

Traditional Chinese Medicine

The conceptual foundation of TCM is entirely different from that of western medicine. TCM is centred on the five solid organs − heart, liver, spleen, lung, and kidney and six hollow viscera − large and small intestine, urinary bladder, stomach, gall bladder, and 'triple burners'. These 'structures' are connected by conduits and vessels with 'Qi' (energy) and blood circulating through them. There is no equivalent counterpart in conventional Western medicine for Qi. TCM treatment is based on the diagnosis of the individual as a whole rather that the Western mainstream medical approach which typically concentrates on the disease. TCM uses a process called 'syndrome identification', whereby the practitioner makes a dynamic conceptualisation of the individual's situation and comes up with a 'pathophysiologic status' (the type of disharmony) for the individual; this status is called 'zheng' or 'syndrome'. The therapeutics used to restore the harmony within the host and between the host and their environment are determined by the identified 'syndrome' [13].

Because TCM views all diseases as patterns of symptoms that correspond to individual disorders or syndromes, the aim is to treat the pattern disorder which is the cause of the problem and not the disease itself. For example, one of the common patterns in acne is “Lung Heat” and is seen as the most common pattern in a teenager. It is important to note that not all patients with acne are treated in the same way. A TCM treatment protocol might include a combination of Acupuncture, Chinese herbs in either raw, tinctured or pill form, external herbal washes or creams and dietary advice.

TCM and Acupuncture

The World Health Organisation recognises acupuncture as a suitable treatment for a wide variety of different conditions [14]. Acupuncture means to puncture with a needle. Acupuncture is usually, but not always, combined with herbal medicine. The needles are small, sterile and disposable. Patients do not normally feel any pain, although they may experience a feeling of warmth, tingling, dull ache or a heavy sensation, which the Chinese call 'sour'.

In many Asian countries, skin diseases are customarily treated with acupuncture. However, there have been very few controlled studies published. In a randomised controlled clinical trial on chloasma, acupuncture had a significantly better effect than vitamins C and E. Some evidence favouring acupuncture treatment of herpes zoster (human (alpha) herpes virus) has been reported. It has been established that acupuncture has an anti-pruritic effect. This has been shown experimentally in volunteers, suggesting that acupuncture could be used in clinical conditions associated with pruritus. Acupuncture with dermal needles has traditionally been used in the treatment of neurodermatitis, with confirmation of its effect in a controlled clinical trial “Treatment of 60 cases of neurodermatitis with three-step seven-star needling therapy”, published in the Journal of Guiyang Chinese Medical College, 1998. Acupuncture, particularly ear acupuncture, has also been used in the treatment of acne vulgaris. In one study published in 2012 a single-blind clinical trial on 84 outpatients with psoriasis vulgaris by auricular therapy (ear acupuncture) combined with a TCM Yin Xie ling Formula, reported reduction scores in the treatment group of 74.4% [14][15].

TCM and Chinese Herbs

The herbal medicine used in TCM can come in various forms. The most common form of prescription involves a selection of herbs specifically chosen for the patient and “cooked”, usually by the

patient as a decoction (tea). The cooking time can be over hours, and most patients find that the actual decoctions are not very palatable. Tinctures are herbal preparations made in alcoholic bases and pills are also prescribed. Up to 8 to 12 pills may be taken twice per day, as the pills are made of herbal plant material, not concentrated chemicals.

In one clinical trial carried out at the Hospital for Sick Children, London, England, a Chinese physician, Dr. Luo, formulated a mixture of 10 herbs for the treatment of atopic dermatitis, consisting of Clematis armandii, Dictamnus dasycarpus, Glycyrrhiza glabra, Ledebouriella satellites, Lophatherum gracile, Rehmannia glutinosa, Paeonia lactiflora, Potentilla Chinensis, Tribulus Terrestris, and Schizonepeta tenuifolia. In this double-blind, placebo-controlled crossover study, there was a clear distinction between the genuine TCM therapy and the placebo herbs. With the active herbs, there was a median decrease in erythema of 91.4% and a decrease in the extent of surface involvement of 85.7% [16].

Washes are decocted herbs that are used externally on the body, usually twice daily. Depending on the herbal prescription proposed the purpose was to assist with various symptoms including extreme itching, heat, ulcerations as well as the healing of the skin.

A 1 - year follow - up with both children and adults who chose to continue to use TCM showed a persistent benefit with only minimal side effects.

This is in contrast to the clinical deterioration of patients who elected to discontinue use of TCM in the ensuing year. It is of interest to note that many of the patients, both children and adults, who chose to continue TCM, were able to decrease the frequency of their TCM to less than daily use, while still others were able to discontinue treatment altogether without experiencing a relapse [16].

TCM and Diet

Dietary therapy in TCM is considered extremely important as all foods possess a certain “nature”, which include Cold, Hot, Sweet, Sour etc., which can affect the body. During a consultation, the TCM practitioner usually advises the patient to avoid certain foods considered to potentially aggravate the condition. The patient is also advised to eat more of the foods that are beneficial for the condition. For example, it is important to avoid hot spicy foods in skin conditions as they create more heat in the body and hence more redness or itching.

Ayurvedic Medicine

Ayurveda originates from India, and the Ayurvedic system of medicine describes a wide range of etiological factors for dermatological disorders. The etiological factors include physical, physiological, psychological, psychosocial, and hereditary and Papakarma (sinful activities) aspect. Ayurveda emphasises threefold therapeutic management based on (avoiding causative factors) for almost all types of disorders including dermatological disorders. Ayurvedic therapy is probably the hardest for non-Indian Practitioners to comprehend as the combined use of herbal formulas with chants, mantras, gems etc. is far more complicated and foreign. Most of the herbs described for the management of dermatological disorders in Ayurveda are “Rasayana drugs” [17].

Various studies on “Rasayana drugs” suggest the following therapeutic properties:

- Immunomodulator
- Adaptogenic
- Antioxidant
- Nootropic
- Antistress

In Ayurveda, “Rasayana drugs” are considered very important for the management of dermatological disorders. Skin health is restored and maintained by directly targeting the different layers and cells of the skin involved in the process of skin ageing & dysfunction and also in the pathogenesis of a disease. Diet modification or dietary supplementation is also very much emphasised in the Ayurvedic system of medicine for the prevention, as well as management, of disorders including skin conditions. The diet rich in Amla (Indian gooseberry), Lavana (salt) and Katu Rasa (pungent, spicy), milk, curd, jaggery (cane sugar), and a diet which is unbalanced should be avoided.

The recommended diet includes old wheat, old barley, pulses like Moonga (brown beans), Masoor (red lentils), Arhar (split pigeon peas), honey, Patola (Luffa cylindrical – vegetable from the gourd family), Neem (leaf), garlic, old Ghrita (ghee) and Tikta Rasa (bitter herbal juices). Also, Triphala (made up of these three fruits, dried and powdered - Amalaki (Emblica officials or Phyllanthus emblica), haritaki (Terminalia chebula) and bibhitaki (Terminalia bellirica)) is important [17].

In Ayurveda, the therapy in the form of “Rasayana drugs” and diets cannot be effective unless the body channels are properly cleansed, and toxic materials are eliminated. Samshodhan (detoxification) is believed to purify or cleanse all the body tissues and bring about the harmony of bio-

humours to obtain long-lasting beneficial effects. So, Ayurvedic practice is to incorporate divine therapy or psychological therapy including chanting Mantras, the spiritual use of herbs and gems, sacrifices, offerings and washing with ceremonial penances, fasting, and other rituals for social wellbeing etc. [17].

There have been published “trials” on the success of Ayurvedic treatments for psoriasis and vitiligo, but these studies are difficult to assess. As an example, in one study patients were randomly divided into two groups. Koshtha Shuddhi was done using Eranda bhrushta haritaki (6g at night with ushnodaka) for both groups for three days before starting the treatment. A total of 111 patients were selected for the study and divided into two groups - A and B. Group A (45) patients were given “Navayasa Rasayana Leha” and “Dhatryadhyo lepa” for the external application while Group B (49) patients were given Medhya Rasayana tablet along with the application of Dhatryadhyo lepa.

The duration of the study was three months, and follow-up was done for one month. Both the groups showed equally good results on improving the quality of life in the patients regarding Dermatology life quality index and Psoriasis disability index.

The study was also coupled with Laboratory investigations and a DLQI and Psoriasis Disability Index (PDI) questionnaire.

1. Blood – Hemoglobin (Hb), total count (TC), differential count (DC), erythrocyte sedimentation rate (ESR), total red blood cells (RBC), and peripheral blood picture.

2. Urine – Routine and microscopic examination.

3. Biochemical – Fasting blood sugar (FBS), serum creatinine, serum glutamate oxaloacetate transaminase (SGOT), serum calcium, total protein, albumin/globulin (A/G) ratio.

The study did not show any PASI scoring nor were the results of the laboratory investigations detailed. The authors only reported on the DLQI and the PDI results. The overall effect on PDI showed that both the therapies had highly significant relief ($P< 0.001$), but percentage wise, group A showed better relief by 72.20% whereas group B showed relief by 65.99%. While DLQI showed beneficial effects of therapy, group A showed 70.26% relief, whereas group B showed 67.64% relief [18].

Western Herbal Medicine (WHM), Naturopathy and Dermatological Conditions Western Herbal Medicine (WHM) covers the following therapies:- Herbal medicine, Phytotherapy, Botanical medicine, Medical herbalism, Herbalism.19 Herbalists are defined as health practitioners who engage in extemporaneous compounding of herbs for therapeutic purposes for individuals under their care and are broadly classified under Western, or European, herbal practice. Two systems of knowledge are identified within

Western herbal medicine: Evidence-based medicine (EBM) and Traditional Knowledge (TK) [20].

EBM has developed as a way to evaluate and generate biomedical knowledge, and to link research findings with clinical application. “Evidence-based medicine is defined as “the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients”. The practice of evidence-based medicine means integrating individual clinical expertise with the best available external clinical evidence from systematic research.” [21].

Traditional Knowledge is used to cover a range of fields, which are referred to as Traditional Ecological Knowledge, Indigenous Knowledge and Folk Knowledge. All of these terms relate to the knowledge which has been developed by indigenous and traditional cultures about their environment [22].

Plants and their secondary metabolite constituents, have a long history of use in modern WHM and certain systems of traditional medicine, and in mainstream medicine are the sources of important drugs such as aspirin (from willow bark), digoxin (from foxglove), quinine (from cinchona bark), and morphine (from the opium poppy) [23].

Since the latter half of the twentieth century, monographs on selected herbs have become available from some sources, including the European Scientific Cooperative on Phytotherapy (ESCOP, 1999), German Commission E (Blumenthal et al., 1998) and the World Health Organization (WHO, 1999).

The WHO monographs classify the herb according to a number of criteria including botanical, synonyms and vernacular names; the herbal part commonly used such as leaf, stem, root, flower etc., its geographical distribution, tests used to identify and characterize the herb (including macroscopic and microscopic examination and purity testing), the active principles (when known), dosage forms and dosing, medicinal uses, pharmacology, contra-indications and adverse reactions.

Other resources that provide detailed information about herbal products in current use include the Natural Medicines Comprehensive Database and the European Commission on herbal medicinal products in the European Union (EU) [24].

Naturopathy

Naturopathy incorporates traditional natural remedies including herbal remedies, nutrition,

acupuncture, traditional Asian medicine, hydrotherapy, and other modalities. Overall, naturopathy focuses on the use of non-toxic, natural remedies. In the US and Canada, Naturopathic Practitioners are trained as family and general physicians and can be registered as doctors. However, in most other countries, this level of training or recognition has not occurred [20]. The tenets of Naturopathy seem worthy:

- First, do no harm
- Use the healing power of nature, the body's innate healing power
- Treat the underlying cause of the disease, not just the symptoms
- Treat the whole person – holistic health
- Educate the patient about their health
- Focus on preventing disease

Some of the modalities involved in Naturopathic Medicine [20], include:

Clinical Nutrition - Naturopathic Practitioner, has the belief that diet is the basis for health, hence encouraging their patients to adopt an appropriate healthy diet, which is the first step towards correcting health problems. Naturopathic Practitioners may use specific individualised diets, fasting, and nutritional supplements.

Lifestyle Counselling and Stress Management - Mental attitudes and emotional states are considered to be important elements in healing and cause of disease. Naturopathic Practitioners are trained in counselling, stress management, hypnotherapy, and biofeedback.

Botanical Medicine - Plants have powerful healing properties. Many pharmaceutical drugs have their origins in plant substances. Naturopathic Practitioners use plant substances in varied forms for their healing effects and nutritional value.

Physical Medicine - Naturopathic medicine includes methods of therapeutic manipulation of muscles and bones. Naturopathic Practitioners may also employ therapeutic exercise, massage, hydrotherapy, bio - electrical therapies, ultrasound, and the use of heat and cold applications.

TCM – Some Naturopathic Practitioners are trained in the fundamentals of TCM and diagnosis. They may use acupressure, and Chinese herbal medicine to promote healing. With additional training and licensure, they may also perform acupuncture.

Homeopathic Medicine - Homeopathic medicines are very small doses of natural substances that stimulate the body's self-healing response with minimal or no side effects. Homeopathy is a popular topic for debate, even from its inception.

Natural Childbirth - In the US and Canada Naturopathic Doctors also offer Natural Childbirth care, provided they undergo additional speciality training. They offer prenatal and postnatal care using appropriate diagnostic and treatment techniques.

Minor Office Procedures - Naturopathic Practitioners with the appropriate training can perform in-office minor surgery including repair of superficial wounds and removal of foreign bodies, warts and cysts with local anaesthesia. Both Herbalists and Naturopaths use their understanding of herbs and dietary modification to treat the body as a whole. They both use a combination of tinctures (usually an alcohol base with herbal infusions), herbal powders and tablets as well as compounded topical creams and lotions. Naturopaths also use nutritional supplementation (mineral, vitamin, amino acids and others) to treat their patients.

An outline of various CAM treatment options for skin conditions including Mode of Action, Properties, Adverse Effects and Drug Interactions follows below:

Traditional Chinese Medicine in Dermatology

Chinese medicine has a long history of treating skin-related symptoms, with previous reviews identifying 174 different herbs that have been used for skin conditions, however western clinical trials and the literature on TCM therapies and formulations for skin conditions, remain scant. Any studies that are published have usually been conducted in China and are often small and uncontrolled. The formulations in these studies are either not specified, or if ingredients are given, then amounts are not, the formulations are not easily replicable outside the study settings and at times the botanical identification of the plant used is obscure as there are no monographs available. This makes it extremely difficult for western research scientists to do follow up and efficacy studies in a controlled setting (Table 1).

Table 1: Example One: Zemaphyte 25, 26, 27, 28

Treatment	Mode of Action and Properties	Ingredients
Oral treatment with daily decoctions	1. Reduction in number of dendritic cells and macrophages in the lesional skin 2. CD1a and CD23 MoDC expression inhibited 3. Allogeneic and autogenic stimulatory activity decreased 4. Induction of IL-10 production	*Ledebouriella saseloides Potentilla chinensis Clematidis armandii Rehmannia glutinosa Paeonia lactiflora Lophatherum gracile Dictamnus dasycarpus Tribulus terrestris Glycyrrhiza glabra Schizonepeta tenuifolia*

A Cochrane review in 2004, collated the reported adverse events from published clinical trials. Blood analysis, renal function and liver function were investigated in all three cross - over trials. No changes were observed for either treatment. A few minor

adverse events were reported with Zemaphyte, including dizziness, gastrointestinal upsets and one case of lichenoid eruption, mild abdominal distension and headaches. However, one serious adverse event resulting in an admission to hospital with a flare of eczema and associated bacterial infection was reported in one trial. Both patients had been taking the herbal tea- bag preparation. Blood tests showed no significant alterations except for one case where lymphocyte count fell transiently and with intermittent lymphopaenia being present for several years. Liver function abnormalities were observed in two children in the follow-up study but became normal after discontinuing the herbal therapy [29].

In one trial, a total of 35 adverse events were reported in 694 patients (5.04%), mainly gastrointestinal symptoms (2.58%) such as nausea, vomiting and mild diarrhoea.

Other adverse events included urticaria, photosensitivity, an exacerbation of eczema, night diuresis, discolouration of teeth and bilirubin creatinine values outside normal limits. Liver function values were raised in seven patients but returned to normal after treatment was discontinued [29].

A topical application using Shi Du Ruan Gao (SDRG) is shown in Table 2. No data was found on adverse events on the constituents of this formula.

Table 2: Example Two: Shi Du Ruan Gao (SDRG) 30, 31, 32

Treatment	Mode of Action and Properties Of some Ingredients*	Ingredients:
Topical twice daily application	*1. Indigo naturalism* has a mode of action which includes anti-inflammatory and antimicrobial. It is thought to modulate the proliferation and differentiation of keratinocytes in the epidermis. Also, it acts as an inhibitor of the infiltration of T lymphocytes. Since these processes are components of subsequent inflammatory reactions in psoriatic lesions, it has a possible application in this field. 2. In mice serum, *Phellodendron chinense* has been shown to significantly downregulate macrophage chemoattractant protein-1 (MCP 1), lipopolysaccharide-induced interleukin-6 (IL-6) and IL- 1β. *Cortex Phellodendri* has also been shown to inhibit inducible nitric oxide synthase (iNOS), activated nuclear factor-κB (NF-κB) by degradation and phosphorylation of IκBα, and attenuated phosphorylation of mitogen-activated protein kinases such as ERK1/2, p38, and JNK in mice treated with lipopolysaccharide. 3. According to TCM theory, Gypsum has astringent and granulating functions. It has been shown in research to promote skin wounds healing by accelerating the formation of micrangium and collagenoblast and the proliferation of granulation tissues.	***I**ndigo naturalis* (Qing Dai) *Cortex Phellodendri* (Huang Bai), Gypsum fibrosum preparatum (Duan Shi Gao) Calamine (Lu Gan Shi) *Galla chinensis* (Wu Bei Zi)

The restriction of access to Chinese clinical trials and databases plus the limited number of western clinical trials drastically reduces the potential to review recorded significant data. The trial data that has been published in western publications and online databases is restrictive and does not allow a definitive ruling on efficacy.

Ayurvedic Medicine in Dermatology

The difficulties outlined earlier in trying to assess. Ayurvedic medicine and clinical trials can be seen in the following example. In a 2013 trial, titled “Comparative effect of Navayasa Rasayana Leha and Medhya Rasayana tablet along with Dhatryadhyo Lepa in Eka kushta (psoriasis)”.

Table 3: Tablet One: Navayasa Rasayana Leha 31, 32, 33, 34, 35

Treatment	Mode of Action and Properties Of some Ingredients*	Ingredients:
Tablet - 2 gm twice a day.	**Dhatri** Reduces elevated levels of serum creatinine, urea nitrogen, TBARS ; decreased iNOS, COX 2 expression. Reduced hexachlorocyclohexane (HCH) & induced raisenin renal gamma glutamyltranspeptidase (GGT) activity. Protects against damaging effects of free radicals, non-radicals and transition metal-induced oxidative stress in the skin. When compared to diclofenac, exhibits anti-inflammatory activity in both acute and chronic model of inflammation. Prevention of immunosuppression through the restoration of phagocytosis and production of gamma-interferon by macrophages. Prevention of chromium-induced oxidative damage through decreased GSH and GPx activity in macrophages. Inhibition of matrix metalloproteinase levels, MMP-1, hyaluronidase activities, and promotion of pro- collagen content in UV-B induced skin photo ageing in fibroblasts by MTT assay. Exhibited a dose-dependent switching from anti- oxidant to pro-oxidant and immuno-modulatory property. Marked up-regulation of anti-inflammatory cytokine (IL-10) concentration. Efficient reduction of pro-inflammatory cytokine (TNF- α and IL-1β) levels. **Haritaki** Immunomodulatory activity of ripe *T. Chebula* fruits – this study showed an increase in the concentration of antioxidant enzymes, GSH, T and B cells. This increase plays an important role in immunity. The occurrence also enhances the concentration of melatonin in the pineal gland and the levels of cytokines. Gallic & chebulagic acid isolated from the extract of herbal medicine, Kashi (myrobalans: the fruit of *Terminalia chebula*) are the active principles that block cytotoxic t lymphocyte (ctl)-mediated cytotoxicity. **Chitraka** In inflammatory immune disorders, *Lumbago zeylanica* extract exhibits immuno- suppressive action. This occurs due these constituents - plumbagin, linoleic acid, nonylnonanoate & stigmasterol. **Bakuchi** The phenolic glycosides in the aqueous extract of *Psoralea corylifolia* inhibits keratinocytes replication in psoriasis. Several flavonoids from *P. corylifolia* exhibit inhibition on IL-6-induced STAT3 activation and phosphorylation and may, therefore, be useful in the treatment of inflammatory diseases	**Dhatri** - *Emblica Officinalis (*Indian Gooseberry) **Aksha** - *Terminalia bellirica* (tropical almond) **Haritaki** - *Terminalia chebula* (another type of tropical almond) **Vidanga** - *Embelia ribes* (flase black pepper) **Chitraka** - *Plumbago Zeylanica* (Ceylon Lead Wort) **Shuddha Bhallataka** - *Semecarpus anacardium* (related to the cashew) **Bakuchi** - *Psoralea corylifolia* **Loha Bhasma** – Iron oxide **Bhrungraj** - *Eclipta prostrata* (false daisy)

*Please Note: the mode of action has been compiled from several studies, reviews and scientific papers

This involved two groups, with each group taking a different tablet formulation (Tables 3 and 4) while both groups used the same topical formulation (Table 5) [31].

Table 4: Tablet Two: Medhya Rasayana 35, 36, 37, 38, 39

Treatment	Mode of Action and Properties Of some Ingredients*	Ingredients:
Tablet – 500 mg 2 tablets twice daily	**Vacha -** A herb which acts on the CNS with anticonvulsant, hypnotic, sedative, and tranquilising properties. After administration for six weeks, *Acorus calamus* resulted in decreased severity of depression as well as improved rehabilitation. It also showed a significant improvement in assessment based on the rating of symptoms on the Hamilton depression rating scale. In an experimental study on rats examining the spontaneous electrical activity and monoamine levels of the brain, the ethanol extract of AC exhibited a depressive action by changing electrical activity and by altering brain monoamine levels in different brain regions. The pharmacodynamic actions of α - Asarone and β - asarone exhibits many similarities to some well-established tranquillisers. A Study of the mechanism of the tranquillising action of α - asarone found that its sedative effect to be dependent on the depression of the ergotropic division of the hypothalamus. In monkeys, α - Asarone produced a prolonged calming effect. In rats, it decreased anxiety and resulted in reduced spontaneous motor activity without dulling perception. Also, it inhibited production of nitric oxide (NO), interleukin - 2 (IL - 2) and tumour necrosis factor - α (TNF-α). Treatment with *A. calamus* extract did not affect intracytoplasmic interferon - γ (IFN - γ) and expression of cell surface markers, CD16 and HLA - DR on human PBMC. It did, however, down-regulate CD25 expression. This study demonstrated the antiproliferative and immuno - suppressive potential of ethanolic extract of *A. calamus* rhizome in vitro. **Jatamansi -** Study results suggest efficacy in the prevention of lipid peroxidation. This is involved in cell membrane disruption and cell damage. The extract showed potential as a powerful oxidant, with high reducing power and inhibition of protein oxidation. It has potential as a scavenger of-of superoxide radicals and ROS. It also decreased DNA damage and protein carbonyls. Also, it is an effective iron chelator. **Jyotishmati -** also has antioxidant properties, and induces antioxidant enzymes. It limits hydrogen peroxide-induced toxicity in neuronal cells.	**Vacha -** *Acorus calamus* (sweet flag) **Haritaki** - *Terminalia chebula* (a type of tropical almond) **Jatamansi -** *Nardostachys jatamansi* (member of the Valerian family) **Jyotishmati -** *Celastrus paniculata* **Yashtimadhu -** *Glycyrrhiza glabra* **Shuddha Bhallataka -** *Semecarpus Anacardium* (related to the cashew) **Guduchi -** *Tinospora cordifolia* (moon seed) **Brahmi -** *Bacopa monnieri* (Waterhyssop) **Shankhpushphi -** *Convolvulus pluricaulis* (Bindweed)

*Please Note: the mode of action has been compiled from several studies, reviews and scientific papers

Unlike most medical dermatological clinical trials conducted on psoriasis, where the use of the Psoriasis Area Severity Index (PASI) scoring system is standard, in this trial the PASI scoring had been altered, and no detail was given on how the psoriasis lesions were assessed. Developed in 1978, PASI is an index used to express the severity of psoriasis, and it combines the severity (erythema, induration and desquamation) and percentage of the affected area to arrive at a final score, as depicted in Table 6.

Table 5: Topical - Dhatryadhyo Lepa 31, 40, 41, 42

Treatment	Mode of Action and Properties of some Ingredients	Ingredients:
Topical **Details as to the exact formulation were not specified, other internet sources – namely a PPT presentation by the authors indicated that the same ingredients as the tablet: Navayasa Rasayana Leha is used. However whether it was a wash, cream, ointment or poultice was not specified.** **It was applied twice daily.**	**Dhatri** A potent antioxidant is limiting oxidative stress-induced damage; it protects against ultraviolet-B irradiation-induced ROS and collagen damage in human dermal fibroblasts. Stimulates proliferation of fibroblasts in a concentration-dependent manner. Induces production of pro-collagen in a concentration and time-dependent manner. Marked decrease of Matrix metalloproteinases (MMP) - 1 production from fibroblasts *E. officinalis* extract acts as an effective agent in collagen metabolism. This enhances its abilities in cosmetic, mitigative and therapeutic applications. **Bakuchi** The extract exhibits antimicrobial activity against both grams positive and gram-negative skin pathogens.	**Dhatri** - *Emblica Officinalis* (Indian Gooseberry) **Aksha** - *Terminalia bellirica* (tropical almond) **Haritaki** - *Terminalia chebula* (another type of tropical almond) **Vidanga** - *Embelia ribes* (flase black pepper) **Chitraka** - *Plumbago Zeylanica* (Ceylon Lead Wort) **Shuddha Bhallataka** - *Semecarpus Anacardium* (related to the cashew) **Bakuchi** - *Psoralea corylifolia* **Loha Bhasma** – Iron oxide **Bhrungraj** - *Eclipta prostrate* (false daisy)

*Please Note: The mode of action has been compiled from several studies, reviews and scientific papers

The authors in the Ayurvedic trial stated that they used a scoring pattern made specifically for their study to assess the pattern of some symptoms, as given by the National Psoriasis Foundation, but do not clarify nor reference it. However, their method for assessment was based on the grades given below:

1. Complete Remission: 100% relief
2. Marked Improvement: 75% to 99% relief
3. Moderate Improvement: 51% to 74% relief
4. Mild Improvement: 25% to 50% relief
5. Unchanged: < 25% or No relief 31

Table 6: Topical - Dhatryadhyo Lepa 31, 40, 41, 42

Score	0	1	2	3	4
Erythema	0 = none	1 =mild	2 = moderate	3= severe	4 = very severe
infiltration	0 = none	1 =mild	2 = moderate	3= severe	4 = very severe
Parakeratosis	0 = none	1 =mild	2 = moderate	3= severe	4 = very severe
Score	0	1	2, 3	4, 5	6
Area 0/0	0	>10	10<30 30<50	50<70 70<90	90<100

This is very different from the universally accepted PASI scoring system. Furthermore, the rating was subjective, using the term “RELIEF”, rather than lesion improvement or clearing. Although Body Surface Area is mentioned, no details were given. Another drawback of the study was the inclusion of both plaque and guttate psoriasis patients, but there were no details as to the number of participants suffering from each type. The authors mentioned that some tests were conducted:

1. Blood – Hemoglobin (Hb), Total count of WBCs (TC), differential count of WBC (DC), erythrocyte sedimentation rate (ESR), Total red blood corpuscles (RBC), Peripheral Blood picture

2. Urine - Routine and Microscopic

examination

3. Biochemical - Fasting blood sugar (FBS), Serum creatinine, serum glutamic pyruvic transaminase (SGPT), Serum calcium, Total protein, the albumin-globulin ratio (A/G ratio) [31].

However, apart from the statement “Insignificant results were found in all laboratory parameters in both the groups”, no further details or actual pre- and post-treatment results were included in the findings.

The difficulty in being able to assess the efficacy of the treatment is due to the inconsistent and confusing reporting parameters. The parameters that were set and reported on have either been modified or do not have a workable translation or equivalent comparison that can be directly related to the western dermatological terminology or parameters used in mainstream clinical trials. Much of the data reported is referring to symptoms and possible modes of action that purely relate to Ayurvedic terminology and thus extremely difficult to properly translate and understand from a western medical point of view.

It was also extremely difficult to obtain safety assessments, adverse effects and contraindications on the majority of the Indian herbs used in this trial, as there are few comprehensive monographs available. A complete monograph for Psoralea corylifolia was the only one found, which included toxicity, acute toxicity, adverse effects, precautions and safety. All other monographs provided very basic information, often without any mention of any toxicity data.

Western Herbal Medicine and Naturopathic Medicine in Dermatology

In Europe, several of the traditional medicines have been studied in clinical trials and developed into modern registered drugs. For a number of these plant-based drugs, controlled clinical trials have proven their efficacy and can thus be prescribed in evidence-based medicine [71]. The European Medicines Agency (EMA) has established a Committee that reports on Herbal Medicinal Products (HMPC).

They issue scientific opinions on herbal substances and preparations, along with information on recommended uses and safe conditions. They require a full quality dossier for all herbal medicinal products as well as other fundamental principles that apply to all medicinal products including good manufacturing practice, pharmacovigilance and requirements on packaging and labelling. They classify herbal medicine products into 1) Herbal substances with Final European Union herbal monographs (alphabetical order) and 2) Herbal substances with Final European Union herbal monographs (according to therapeutic areas).

The lists are also divided into two groups of herbal medicinal products: a) well - established use: demonstrated with sufficient safety and efficacy data and b) traditional use: accepted by adequate safety data in conjunction with plausible efficacy.

For this paper, a few herbs have been selected, including Calendula Officinalis L., Melaleuca alternifolia, Myrrha, Centella Asiatica (L.) (Gotu Kola) and Aloe Vera to show their mode of action, interactions and adverse effects as discussed in Table 7.

Each of these herbs has been used as topical treatments in some clinical trials for various wound healing and skin conditions with differing results. Usually, the clinical trials are on the single herb at various doses and in various carriers, including creams, gels, and petroleum bases. This makes it exceptionally difficult to quantifiably state that a certain percentage of herbal extract “Y” is consistently efficacious in resolving a certain skin condition. Much research time and effort have been spent in trying to identify the active ingredients and therapeutic properties, including antimicrobial, antioxidant, and antiseptic.

In 2006, an evidence-based systematic review by the Natural Standard Research Collaboration was conducted on calendula. They concluded that much of the research had been done on animals and as such may be of limited use only when assessing viability in treating skin conditions. However, while recognising that traditionally, calendula has been used topically for treating minor wounds, burns and other skin problems, they found that there was no strong scientific evidence to support this use.

However, they felt that there was good scientific evidence to support the use of calendula in Radiation dermatitis [61]. Calendula can prevent oxidative stress, making it theoretically an ideal treatment for radiodermatitis. It is thought that this occurs via the numerous polyphenols contained in its extract. Polyphenols have many potentially therapeutic roles as antioxidants on the skin. The pylene glycol extract of Calendula has been studied, with results showing that it interferes with neutrophil radical oxygen species (ROS) and radical nitrogen species (RNS) generation, particularly nitric oxide, at concentrations as low as 0.2 μg/mL [46].

Table 7: Properties of selected herbs

Treatment Topical	Adverse Effects	Drug Interactions	Mode of Action and Properties
***Calendula Officinalis* L.** **46, 47, 48, 49, 50**	No allergic events occurred in the group (126 patients) given Calendula during the clinical trial. There is no evidence for phototoxic activities. The extract was found to cause allergy in 9 patients out of 443 (2.03 %) when assessed by patch testing method. Therefore a cross-sensitivity with other members of the Asteraceae cannot be excluded. Experimentally, the plant extract is a weak sensitiser. This is probably due to the lack of sesquiterpene lactones in Calendula flowers.	None reported	The polysaccharides isolated from an aqueous extract of *Calendula* flowers stimulates the phagocytosis of human granulocytes. *Calendula* flower extracts have been shown to exhibit anti - oxidative effects on liposomal lipid peroxidation induced by Fe + and ascorbic acid. *Calendula* extract contains numerous polyphenols which inhibit oxidative stress, At concentrations as low as 0.2 µg/mL, *Calendula* exhibits anti - oxidant qualities. It interferes with neutrophil radical oxygen species (ROS) and radical nitrogen species (RNS) generation, particularly nitric oxide *Calendula* inhibits lipoxygenase activity in vitro. It also significantly reduces monocyte chemotactic protein - 1, keratinocyte-derived chemokine, granulocyte colony-stimulating factor, IL - 1 alpha, and vascular endothelial growth factor (VEGF). Calendula exhibits anti-inflammatory activity via its active components - triterpenoids, faradiol monoester and free ester faradiol. Of these, the latter is the most active and exhibits the same effects as an equimolar dose of indomethacin. The extract of *Calendula* reduced pro-inflammatory markers including TNF - α, IL - 1β, (IL - 6), interferon-gamma (IFN - γ), c - reactive protein (CRP), and cyclooxygenase - 2 (COX - 2).
Melaleuca alternifolia **46, 47, 48, 49, 50**	Adverse skin reactions have been reported. These include mild pruritus, burning sensation, discomfort, irritation, stinging, erythema, and oedema. Allergic reactions have been reported. The frequency is not known. In rare cases, a burn - like skin reaction has been reported. Considerable systemic exposure may result from percutaneous absorption after topical application of Tea Tree oil and Tea Tree oil-containing products. This may occur especially when neat oil, body lotion and foot spray/powder is used (see appendix). The extent of systemic exposure to Tea Tree Oil from cosmetic products is uncertain due to inadequate availability of dermal absorption studies. In accidental poisonings, *Melaleuca aetheroleum* causes Central Nervous System depression and muscle weakness. These symptoms resolved within 36 hours. Classified as hazardous - R22 Harmful if swallowed - Swallowing can result in hallucinations, ataxia, diarrhoea, central nervous system depression, sleep or coma.	None reported	**Tea Tree Oil (TTO) -** suppresses inflammatory mediator production through activated human monocytes. These include lipopolysaccharide - induced tumour necrosis factor-α, IL-1β, IL-8, IL-10 and prostaglandin E2. Of these, lipopolysaccharide-induced tumour necrosis factor-α is often considered the most influential inflammatory cytokine. The water-soluble components of TTO can suppress the production of superoxide by human monocytes, but not neutrophils activated in vitro. TTO may enable neutrophils to be fully active in an acute inflammatory response and eliminate foreign antigens while suppressing monocyte production of superoxide and inflammatory mediators. It thereby prevents oxidative damage and the activation of other cells that are seen in more chronic inflammatory states. Micro-emulsion (stable dispersions of oil and water stabilised by an interfacial film of a surfactant, usually in combination with a co-surfactant) systems of 5% TTO from M*elaleuca alternifolia* are promising vehicles for transdermal drug delivery. The major component of TTO is Terpinen-4-ol. It has shown strong antimicrobial and anti-inflammatory properties. In vitro research has demonstrated that terminal-4-ol can inhibit the production of several inflammatory mediators (such as interleukins) by human peripheral blood monocytes.
Commiphora myrrha **51, 52, 53, 54, 55**	Allergic contact dermatitis has been reported.	Interaction with warfarin has been reported. –the anticoagulant effect of warfarin was reduced after aqueous extract of boiled roots of *Commiphora molmol* was taken orally. When taken orally, Gugulipid, a constituent of Myrrh, decreased the serum level of the drugs Diltiazem and Propranolol. Another component, *Z*-guggulsterone, increased the uptake of iodine by the thyroid gland as well as oxygen uptake in the liver and bicep tissues. This occurred when taken orally combined with some thyroid medications. Oral administration of myrrh may potentiate the effects of aspirin, non-steroidal, anti-inflammatory drugs, and warfarin. Oral guggulsterone was found to be a bile acid receptor and farnesoid X	Several sesquiterpenes (furanodesma-1.3- diene, current, furanodiene, furanodiene-6-one and metyhoxyfuranoguaia-9-one-8-one) have been found to have antibacterial, antifungal, analgesic and local anaesthetic effects. As demonstrated in vitro, myrrh contains terpenes with fairly potent antibacterial effect against several bacteria including the most common wound pathogen *S. aureus.* The mechanism of action is unknown. The phytochemical evaluation showed the presence of alkaloids, glycosides, steroids, terpenoids and flavonoids in the methanol extract of guggul. Flavonoids are the key metabolic compounds having anti-inflammatory, antihistaminic, antibacterial and antiviral properties. It has also shown a moderate scavenging effect against 2,2-diphenyl-1-picrylhydrazyl (DPPH) radicals. Guggul shows a definite pro-healing action due to the wound contraction ability of the oil and resin of scented myrrh. One reason for this ability could be via the enhanced proliferation of epithelial cells. As an incision wound treated by guggul shows greater tensile strength, it might be inferred that myrrh extracts not only increase collagen synthesis per cell but also aid in cross-linking of the proteins. This wound healing activity is likely to be attributed to its high content of terpenoids. Due to their astringent and antimicrobial properties, terpenoids are known to promote the wound healing process. This process could be responsible for wound contraction and increased rate of epithelization. Another component, sesquiterpene lactones, is known to possess antioxidant activity. This may contribute to the wound healing process and the promotion of rapid wound healing.

		receptor (FXR) antagonist both in vitro and in vivo. Topically–None known	
Centella Asiatica (L.) (Gotu Kola) ***56, 57, 58***	Administered in the recommended doses, C. asiatica is not toxic, and side effects are rare. When used externally, it may cause allergic reactions and burning. The sensitising effect of the triterpene fraction could be a potential cause of allergic contact dermatitis.	None Identified	*C. asiatica* affects extracellular matrix proteins deposition. It stimulates fibroblasts proliferation, activates the Smad pathway, increases collagen synthesis and decreases the activity of metalloproteinases, thereby increasing collagen deposition.
Aloe Vera Topical 59	Possible erythema, burning and stinging. Generalized dermatitis may occur in sensitive individuals. Anthraquinones, such as aloin and barbaloin, may cause allergic reactions.	None Identified	Topical and oral Aloe vera results in significantly increased collagen synthesis. This occurs due to two active components - Glucomannan, a mannose-rich polysaccharide, and gibberellin, a growth hormone. These interact with growth factor receptors on the fibroblast, thereby stimulating its activity and proliferation. Similarly, Aloe gel increases the collagen content in wounds and increases collagen composition type III. Collagen cross-linking is also stimulated. Wound contraction accelerated and resultant scar tissue is improved. After oral or topical treatment, the synthesis of hyaluronic acid and dermatan sulfate in the granulation tissue of a healing wound is increased. Aloe vera gel has been reported to have a protective effect against radiation damage to the skin. When aloe vera gel is applied to the skin, metallothionein (an antioxidant protein), is generated in the skin. This scavenges hydroxyl radicals and prevents suppression of superoxide dismutase and glutathione peroxidase in the skin. This also prevents UV-induced suppression of delayed-type hypersensitivity, via the decreased production and release of skin keratinocyte-derived immunosuppressive cytokines such as interleukin-10 (IL-10). Aloe vera inhibits the cyclooxygenase pathway and reduces prostaglandin E2 production from arachidonic acid. Recently, the novel anti-inflammatory compound called C-glucosyl chromone was isolated from gel extracts. Aloe stimulates fibroblast which produces collagen and elastin fibres, resulting in more elastic and less wrinkled skin. Its cohesive effects on the superficial flaking epidermal cells soften the skin. The amino acids in Aloe also soften hardened skin cells, and due to its zinc content, it acts as an astringent to tighten pores. Its moisturising effects have also been studied in the treatment of dry skin associated with occupational exposure where *aloe vera* gel gloves improved skin integrity, decreased the appearance of fine wrinkles and decreased erythema. It also has an anti-comedonal effect. *Aloe vera* contains six antiseptic agents with an inhibitory action on fungi, bacteria and viruses - Lupeol, salicylic acid, urea nitrogen, cinnamonic acid, phenols and sulfur.
***Centella Asiatica*(L.) (Gotu Kola)** Oral **56, 57, 58**	In recommended doses, orally administered *C. asiatica* may cause dyspepsia, nausea and headache. Exceeding the recommended dosage may result in dizziness and drowsiness. In diabetic patients, Gotu Kola may cause hyperglycaemia, whereas, in existing hyperlipidemia, elevated lipid levels may occur. When administered for 20– 60 days, there is increased the risk of hepatotoxicity of *C. asiatica* in humans. Due to its emmenagogic effects, the oral administration of Gotu Kola is to be avoided during pregnancy and lactation.	Medications for Diabetes and hyperlipidemia may need to be modified.	When administered orally, Asiaticoside, a constituent of *C. asiatica*, exhibited potent antipyretic and anti-inflammatory effects in lipopolysaccharide-treated rats. These effects could be associated with the inhibition of liver myeloperoxidase activity, a decrease of pro-inflammatory mediators, such as TNF-α and IL-6 levels, and inhibition of COX-2 protein expression and PGE2 production. Asiaticoside increases the level of anti-inflammatory IL-10 in serum and up-regulates heme oxygenase-1 (HO-1) expression, an enzyme which protects the liver. The presence of glycosides like asiaticoside, madecassoside as well as triterpenes in *Centella Asiatica* may help to explain its antiallergic, anti-pruritic as well as anti-inflammatory activities. Of these components, glycosides possess antioxidant, antiviral, antiallergic, and anti-inflammatory activities. Certain glycosides possess potent inhibitory activities against a wide array of enzymes - protein kinase C, protein tyrosine kinase & phospholipase A2. Other glycosides potentially inhibit prostaglandins, a group of pro-inflammatory signalling molecules. This is mainly due to inhibition of key enzymes involved in prostaglandin biosynthesis (lipoxygenase, phospholipase and cycloxygenase). This action provides the mechanism by which glycosides act as an anti-inflammatory. Analgesic is als associated with glycosides as well as with terpenes.
***Aloe Vera* Oral -60, 62**	(Group 2B). possibly carcinogenic to humans Known hypersensitivity to the active substance. Oral - Cases of intestinal obstructions and stenosis, atony, appendicitis, inflammatory colon diseases (e.g. Crohn's disease, ulcerative colitis), abdominal pain of unknown origin, severe dehydration - water and electrolyte depletion have been reported. Aloes should not be administered in cases of faecal impaction, acute or persistent gastro-intestinal complaints, for example, abdominal pain, nausea and vomiting. Possible electrolyte imbalance in patients with kidney disorders.	Patients taking cardiac glycosides, anti-arrhythmic medications, QT- prolongation medications, diuretics, adrenocorticosteroids or liquorice root, have to consult a doctor before taking aloes concomitantly.	After oral *Aloe* Vera administration, two of its components - Glucomannan (a mannose-rich polysaccharide) and gibberellin (a growth hormone) interact with growth factor receptors on the fibroblast. This stimulates the fibroblast's activity and proliferation, resulting in significantly increased collagen synthesis. Following oral administration of Aloe, increased synthesis of hyaluronic acid and dermatan sulfate in the granulation tissue of a healing wound has been reported.

The Need for a New and Different Approach

In the 80's the need for a new and different approach became more and more apparent, as neither mainstream nor CAM seemed to be fulfilling the needs of the patient. In the past, both CAM and mainstream medicine remained at opposite ends and were never to interact. In the 80's, Dr Michael Tirant saw the opportunity to bring the two closer together, especially in the treatment of dermatological conditions, where he had developed very effective treatment protocols, including the use of bio - herbal actives.

The question was: "How could CAM and allopathic medicine be brought together to offer a more effective treatment approach, which has more longterm benefits for the patients?"

For a longterm solution to psoriasis or other dermatological conditions for that matter, it is vital to identify triggers of these conditions and understand the pathways of how they elicit a flare-up. His research identified many triggers, including drugs, infections, trauma, chemicals, alcohol, smoking, hormones, stress, diet, and lifestyle issues.

Interestingly, some of these triggers initiate a flare - up while others continue to exacerbate the condition. Scientific reports (internal publications) were written on individual triggers and circulated to doctors. Lectures and talks were organised at doctors' clinics and seminars to promote his findings. Unfortunately, he was not able to publish his findings as most journals declined publication because the findings were not scientific or legitimate.

He spent many years working on bacterial superantigens - how they could elicit a flare - up in psoriasis, and how they could be targeted using bio-herbal therapies. Many of the herbs that were tested during the initial stages possessed anti-inflammatory, antioxidant, anti-microbial (viral/bacterial/fungal), anti-pruritic and analgesic properties.

This brought in a very scientific and medical approach that resonated with doctors and formed a stepping stone for collaboration. The outstanding results achieved with patients helped to open doors, both in Australia and overseas, and brought more acceptance and credibility for his treatments.

Although there was a reluctance for his work initially, the medical fraternity has, over the years, started to accept that Tirant's protocols are effective in the treatment of many skin diseases. In Australia, doctors in Integrative practices started to incorporate his treatments with orthodox drugs and so began Integrative Dermatology in Australia. His treatment protocols are now used by patients and doctors in many countries around the world. His work is well published in collaboration with international dermatologists, through international clinical trials and confirmation of the efficacy of his treatments [63][64][65][66][67][68]69][70][71][72][73][74][75][76][77][78][79][80][81][82]. Interestingly, there are now also many publications confirming Tirant's findings on triggers of psoriasis.

His motto is – "we target the triggers and treat the symptoms". He has developed over 40 topical formulations for symptomatic relief and over 25 oral supplements to target triggering factors of many dermatological conditions including psoriasis, eczema, ichthyosis, rosacea, fungal infections and acne. The treatments are now used in many countries around the world.

The exact combination of herbal ingredients, specifically the essential oils, is carefully chosen for the treatment of a skin condition and is based on the therapeutic properties and bioactive plant compounds of the various ingredients. This creates a synergistic compounding effect of the actives that work on specific pathways.

Essential oils are highly complex mixtures of volatile compounds with some containing more than 100 different components. The major volatile constituents are hydrocarbons (pinene, limonene, bisabolene), alcohols (linalool, santalol), acids (benzoic acid, organic acid), aldehydes (citral), cyclic aldehydes (criminal), ketones (camphor), lactones (bergaptene), phenols (eugenol), phenolic ethers (anethole), oxides (1, 8 cineole) and esters (geranyl acetate). All these compounds may be classified into two main categories: terpenoids and phenylpropanoids.

Essential oil compounds are fat - soluble, and thus they had the ability to permeate the membranes of the skin before being captured by the micro-circulation and drained into the systemic circulation, which reaches all targets. Currently, no one study gives a clear explanation of the mode of action of essential oils. Given the complexity of their chemical composition, it would suggest a complexity that makes it difficult to identify the overall molecular pathway of action(s). It is quite possible that each of the constituents of essential oils may have its mechanism of action [83]

That said, there are several proposed cellular actions or mechanisms that may explain the anti-inflammatory activity of medicinal plants that have been observed in vivo. These mechanisms include anti-oxidative and radical scavenging activities, regulation of cellular activities of the inflammation-related cells - mast cells, macrophages, lymphocytes, and neutrophils. They have many actions including inhibition of histamine release and T - cell proliferation.

Table 8: Sominex - topical for treatment of psoriasis. Note: only a small number of the essential oils were discussed due to the long list of ingredients

Treatment	Mode of Action
Topical –	
83, 84, 85, 86, 87, 88, 89,	Zinc is required for collagen, and protein synthesis as low levels of zinc are associated with impaired wound healing.
90, 91, 92	Zinc is also required for cellular growth and replication and may assist in wound healing by reducing free radical activity and inhibiting bacterial growth.
Ingredients include: Zinc oxide Salicylic acid Sweet almond Oil Jojoba Seed Oil Avocado Oil Carrot Seed Oil Calendula extract Orange Oil Wheat germ Oil Apricot kernel Oil Lavender Oil Sandalwood Oil Patchouli Oil Emu Oil Bergamot Oil Rosemary oil Geranium Oil Evening primrose Oil Eucalyptus Oil Pine needle oil Chamomile oil Myrrh Oil Neroli Oil	Zinc serves as a cofactor in numerous transcription factors and enzyme systems including zinc-dependent matrix metalloproteinases (MMP). These augment auto-debridement and keratinocyte migration during wound repair.
	Zinc confers resistance to epithelial apoptosis through stabilising cellular membranes. It protects cells against reactive oxygen species (ROS) and bacterial toxins through anti - oxidant activity of cysteine-rich metallothioneins (MT) and superoxide dismutase.
	Salicylic acid facilitates desquamation by solubilising the intercellular cement that binds scales in the nail plate, thereby loosening the keratin and facilitating the penetration of other medicaments into the nail plate.
	The keratolytic effect of Salicylic acid may also provide an antifungal action because the disruption of the keratin also suppresses fungal growth. It also aids in the penetration of other antifungal agents.
	Salicylic acid also has a mild antiseptic action and possesses anti - inflammatory, ant I -pruritic, analgesic and antimicrobial properties. Its anti-inflammatory and analgesic action appears to be mediated by the inhibition of prostaglandin synthesis via the inhibition of the cyclooxygenase enzyme.
	Many of the essential oils are known for their hydrophobicity, which enables them to partition the lipids of the bacterial cell membrane and mitochondria. This disrupts the cell structures and renders them more permeable.
	Extensive leakage from bacterial cells or the exit of critical molecules and ions will lead to their demise.
	In general, it is proposed that most essential oils target microbial cell membranes, affecting their integrity or permeability or compromising membrane-associated functions (primarily respiration). This leads to fungal cell wall polymer degradation, membrane channel and pore formation, and damage to ribosomal inhibition of DNA synthesis and the cell cycle. Almost all of the essential oils have some antibacterial/antifungal functionality.
	Many of these essential oils are also known for their antioxidant properties. This is most often due to phenolic acids (gallic, protocatechuic, caffeic and rosmarinic acids), phenolic diterpenes (carnosol, carnosic acid, rosmanol, and rosmadial), flavonoids (quercetin, catechin, naringenin and kaempferol), and volatile oils (eugenol, carvacrol, thymol and menthol).
Topical –	
112, 113, 114, 115, 116,	Essential oils can inhibit the expressions of pro-inflammatory cytokines (IL-1β, IL-6 and TNF-α), cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS).
117, 118, 119	They can also increase the expression of anti-inflammatory cytokine IL-10 and inactivate nuclear transcription factor κappa B (NF-κB).
Zinc oxide Salicylic acid Sweet almond Oil Jojoba Seed Oil Avocado Oil Carrot Seed Oil Calendula extract Orange Oil Wheat germ Oil Apricot Kernel Oil Lavender Oil Sandalwood Oil Patchouli Oil Emu Oil Bergamot Oil Rosemary oil Geranium Oil Evening primrose Oil Eucalyptus Oil Pine needle oil Chamomile oil Myrrh Oil Neroli Oil	Chamomile oil contains alpha-bisabolol, which oxides A & B, and matricin (usually converted to chamazulene) and other flavonoids. These possess anti-inflammatory and antiphlogistic properties.
	A study in human volunteers demonstrated that the flavonoids and essential oils in chamomile penetrate below the skin surface into the deeper skin layers.
	This is important for its use as a topical antiphlogistic (anti-inflammatory) agent.
	One of the chamomile's anti-inflammatory activities involves the inhibition of LPS-induced prostaglandin E(2) (PGE2) release and attenuation of cyclooxygenase (COX-2) enzyme activity without affecting the constitutive form, COX-1.
	The polyphenols in chamomile oil exhibit anti-inflammatory effects due to the inhibition of pro-inflammatory biomarkers in THP1 macrophages. These can reduce inflammation in neurovascular units (NVU) at the site of migraine pain.
	Chamomile has neuro-protective effects because of the induction of reduced tissue NO levels.
	In vivo analysis of patchouli found that its anti-inflammatory activity occurred due to the regulation of mRNA expression of a panel of inflammatory mediators.
	These include TNF-α, IL-1β, iNOS and COX-2. Inhibition of COX-2 produces the analgesic, antipyretic, and anti-inflammatory effects typical of non-steroidal anti-inflammatory drugs (NSAIDs).
	Various essential oils or their constituents inhibit cytokine production. For example, a constituent of many essential oils, 1,8-cineol, inhibited TNF-α and IL-1β in human lymphocytes, α-humulene reduced TNF-α production and terpinen-4-ol suppressed the production of TNF-α, IL-1β,
	IL-8, IL-10 and PGE2 by LPS-activated monocytes.
	A constituent of Eucalyptus Oil,1.8-cineole (eucalyptol), has been reported to inhibit the production/synthesis of TNF-α, interleukin-1, leukotriene B4, and thromboxane B2 in inflammatory cells. Similar to acetylsalicylic acid, it also inhibits the production of prostaglandins and thromboxanes.
	The mechanism of the analgesic effects of the eucalyptus oils is not known. It is speculated that it may be linked to processes involved in the prevention of sensitisation of the nociceptor, down-regulation of the sensitised nociceptor and/or blockade of the nociceptor at peripheral and/or central levels.
	Eucalyptus oil effectively inhibits neutrophil migration as well as carrageenan-induced oedema.
Topical –	
112, 113, 114, 115, 116,	The main constituents of the resin from which Myrrh Oil is obtained are boswellic acids, which have been found to inhibit the synthesis of leukotrienes (inflammatory compounds produced when oxygen interacts with polyunsaturated fatty acids).
117, 118, 119	Boswellic acids have been found specifically to inhibit 5- lipoxygenase, the key enzyme of leukotriene biosynthesis. Leukotrienes, a family of lipid mediators, play a key role in the pathogenesis of inflammation.
Zinc oxide Salicylic acid Sweet almond Oil Jojoba seed Oil Avocado Oil Carrot Seed Oil Calendula extract Orange Oil Wheat germ Oil Apricot Kernel Oil Lavender Oil Sandalwood Oil Patchouli Oil Emu Oil Bergamot Oil Rosemary oil Geranium Oil Evening primrose Oil Eucalyptus Oil Pine needle oil Chamomile oil Myrrh Oil Neroli Oil	

They also modulate the enzymatic activities of arachidonic acid (AA) metabolising enzymes, such as phospholipase A2 (PLA2), cyclooxygenase (COX1 and COX 2), and lipoxygenase (LOX) and the nitric oxide (NO) producing enzyme, nitric oxide synthase (NOS). All of these pathways are involved in the activation and exacerbation of skin conditions [84].

An example of the ingredients contained in the topical treatment for psoriasis is shown in Table 8.

Oxidative stress is involved in the pathogenesis of psoriasis. In psoriasis, studies have revealed increased markers of oxidative stress and decreased antioxidant capacity in plasma, in white blood cells and skin.

The comprehension of the role of immune function in psoriasis could permit the management of this complex disease, which dramatically affects patients far beyond the skin. In fact, cytokines and growth factors released by activated T cells have been shown to display a prominent role in keratinocyte formation. Six of the essential oils in Dr Michaels® (Soratinex®) family of products (calendula, patchouli, geranium, neroli, myrrh (OME)), were studied for redox status of fibroblast primary culture from lesional psoriatic skin hyperproliferation.

The study focused on dermal fibroblasts, which are involved in the accelerating keratinocyte proliferation of developing psoriatic lesions. According to the results, the total antioxidant capacity of OME (at the 1:5000 dilution) resulted equivalent to 163.6mM Trolox, which indicated a very high antioxidant capacity for the provided oil mixture [93].

The preliminary experiment aimed at evaluating the effect of OME on cell viability. A further dose-dependent test was carried out in psoriatic fibroblasts in the presence of increasing OME concentrations ranging from 1:1000 to 1:10000. The results indicated that treatment with 1:5000 OME increased the viability of psoriatic fibroblasts by 37.9 ± 1.7% compared to untreated cells.

A significant decrease in intracellular ROS production was observed in OME-treated fibroblasts compared to untreated fibroblasts as revealed by confocal analysis [93].

The results indicated a strong protective, redox balancing effect of OME obtained from the vegetable oil mixture (Dr Michaels® Soratinex® family products) and if used at an appropriate concentration, significantly increases the viability and decreases intracellular ROS production in human psoriatic fibroblasts. A strong antioxidant effect of the OME obtained from Dr Michaels mixture of oils may be a reason for the effectiveness of the mixture in the topical treatment of psoriasis [93].

The oral supplement range consisted of a specific combination of herbs, either leaf, bark, root, stolen or bulb. The normal dose is one tablet twice daily, however for short periods in the acute stage, two tablets twice daily may be prescribed for 3 - 4 weeks.

Conclusion

Although initially considered unscientific, today many herbs have been scientifically trialled to elucidate their efficacy, mode of action and possible adverse events for them to be safely combined with modern medicine.

Today Integrative Dermatology is well-accepted internationally with many new practices starting in many countries, such as the USA.

Many integrative dermatologists combine integrative approaches in their clinics; such as minerals, herbal products, stress management techniques and clinical nutrition, to achieve the best outcomes for their patients.

These practitioners now realise that the best approach is one where the appropriate triggers for each patient are considered, as each is unique.

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