Herbal Biomedicines for Dermatological Disorders

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Herbal extracts and isolated plant compounds play an increasing role in the treatment of skin disorders and wounds. Several new herbal drugs, medicinal products and cosmetic products for the treatment of various skin conditions have been developed in recent years.

Keywords: atopic dermatitis ; psoriasis ; wound healing

1. Introduction

Herbal therapies have been used for the treatment of skin conditions for centuries. Several plant compounds are still used in topical treatments, such as salicylic acid from willow bark from *Salix* spp. (for desquamation), 8-methoxypsoralen from *Ammi visnaga* (L.) Lam. (for photochemotherapy), and tannins from oak bark, black tea or hamamelis bark (for oozing eczema). Traditionally used medical plants were evaluated and documented in 300 monographs by Commission E at the German institute for drugs and medicinal products (BfArm) between 1976 and 1993. About 30% of these plants received a negative evaluation. The positive monographs contained 25 plants with relevance for dermatological treatments. They include well-known medical plants such as chamomile, which hazel and marigold. However, most of these plants only achieved a low level of evidence for their efficacy, because only a few high quality clinical studies have been performed [1][2] During the last years the therapeutic potential of medical plants traditionally used in dermatology has been explored, and some of them have been developed and approved as drug or medical device for the treatment of skin disorders, e.g. for atopic dermatitis, psoriasis and wound healing.

2. Atopic Dermatitis

Atopic dermatitis (AD) is a chronic, pruritic inflammatory skin disease. Dermatologists often prescribe glucocorticoids to the patients, but patients and parents of children with AD worry about the side effects of glucocorticoids, especially in long term therapy. They ask for herbal therapies because they expect similar effectivity and fewer side effects. A comprehensive, evidence-based review on clinical studies with herbal products for AD has been published recently [3]. Some of the studies are highlighted here.

2.1. St. John’s Wort (Hypericum perforatum (L.))

St. John’s wort is traditionally used as hypericum oil for the treatment of wounds and burns. The lipophilic phloroglucin derivative hyperforin displays antibacterial, anti-inflammatory and keratinocyte differentiation-promoting properties [4].

2.2. Licorice (Glycyrrhiza glabra (L.))

The anti-inflammatory effect of licorice (*Glycyrrhiza glabra* L. and *Glycyrrhiza uralensis* Fisch. ex DC.) is well studied and summarized in an actual review [5]. Most studies were performed with the triterpenes glycyrrhizin and glycyrrhetinic acid of licorice on skin [5][6][7]. However, other ingredients, such as the flavonoid isoliquiritigenin [8] and the chalcone licochalcone A [9] [10][11] display also anti-inflammatory effects.

2.3. Tormentil (Potentilla erecta (L.))

Tannins from black tea (*Camellia sinensis* (L.) Kuntze), witch hazel (*Hamamelis virginiana* L.) and oak bark (*Quercus* spp.) have been empirically used in dermatology since ancient times. Tannins are used as wet-lipid wraps or local baths for the treatment of acute, oozing eczema. A cream containing 2 % tannins from the rhizome of tormentil (*Potentilla erecta* (L.) Raeusch.) displayed a corticoid-like vasoconstrictive effect in an occlusive patch test after 48 hours [12].

2.4. Bitter substances

Bitter substances have been used as appetizing and digestion promoting agents since Ayurvedic medicine 5000 years ago. Only recently the molecular structure of bitter taste receptors (TAS2Rs) has been elucidated, and it was shown that TAS2Rs are also expressed in human epidermis [13]. Bitter compounds such as salicin from willow bark (from *Salix* spp.) and amarogentin from *Gentiana lutea* (L.) bind to the bitter taste receptors of the skin, eventually leading to calcium influx and the enhanced expression of skin barrier-constituting proteins such as filaggrin [13].

2.5. Evening Primrose (*Oenothera* biennis (L.))

The oil obtained from evening primrose seeds is beneficial for AD due to its high content of γ-linolenic acid. It is used both internally and in topical products. Only a few high-quality studies have investigated the effect of evening primrose oil in AD.A recent meta-analysis of the existing literature concludes that there is a moderate effect of evening primrose oil on itching, scaling and crusting in AD [14].

3. Psoriasis Vulgaris

Herbal products are also used for the topical treatment of psoriasis. Psoriasis is a chronic, immune-mediated skin disease that shows red and scaly patches on the skin that itch or burn. Three systematic reviews have evaluated the use of herbal therapies in psoriasis [15] [16] [17].

3.1. Araroba Tree (Vataireopsis araroba (Aguiar) Ducke)

The most potent topical treatment for psoriasis is the anthracen derivative dithranol (synonym: anthralin). It was obtained from chrysarobin, extracted from the bark of the araroba tree that grows in the rain forests of the Amazon. Dithranol inhibits the release of pro-inflammatory cytokines and the proliferation of keratinocytes.

3.2. Lace Flower (Ammi majus(L.) and Ammi visnaga (L.))

The furanocoumarins 8-methoxypsoralen (8-MOP) and 5-methoxypsoralen (5-MOP) are isolated for therapeutic use from *Ammi majus* (L.) and *Ammi visnaga* (L.) Lam. The psoralens are phototoxic substances that are photo-activated by long-wave ultraviolet A (UVA) radiation and may cause severe phototoxic skin reactions.

3.3. Barberry Bark (Mahonia aquifolium (Pursh) Nutt.)

The barberry *Mahonia aquifolium* is a shrub indigenous to Northern America. It was used for centuries by Native Americans to treat psoriasis. Tinctures and ointments from *Mahonia* bark are available as traditional drugs in Northern America and Europe.

3.4. Indigo (Baphicacanthus cusia, Brem.)

‘Indigo naturalis‘ is an important remedy in Traditional Chinese Medicine (TCM). It is a blue powder obtained from the plant *Baphicacanthus cusia* by grinding, fermentation and addition of lime. In a randomized placebo-controlled study 42 patients suffering from chronic plaque psoriasis were treated once daily with a 10% indigo containing ointment for 12 weeks. The indigo naturalis used contained 1.4% indigo and 0.16% indirubin. Treatment with indigo improved symptoms by 81%, while the improvement with placebo was only 26% [18].

3.5. Turmeric (Curcuma longa (L.))

Turmeric plays an important role in TCM and in Aryuvedic Medicine. In vitro, turmeric and its major active ingredient curcumin display anti-inflammatory, antimicrobial and anti-oxidative properties [19]. During the last years some laboratory and clinical studies have investigated the therapeutic potential of curcumin in psoriasis. Curcumin may improve psoriasis by inhibition of phosphorylase kinase [20] [21], downregulation of pro-inflammatory cytokines such as IL-17 and TNF-α, as well as improvement of the epidermal barrier by inducing the expression of involucrin and filaggrin *in vitro* [22].

3.6. Olibanum (Boswellia Serrata, Triana & Planch.)

Olibanum containing ointments were recommended in the Greco-Roman period by Hippocrates, Galen and Dioscorides for the treatment of various skin disorders such as psoriasis, burns, warts, bleeding and wounds. Recently 200 patients with mild to moderate psoriasis were treated in an open label application study three times daily for 12 weeks with an olibanum ointment containing 5 % *3-O-Acetyl-11-keto-β-boswellic acid*. The PASI was significantly reduced, as well as serum biomarkers such as leukotrien B4, TNF-α, VEGF and PGE_2 . Thirteen patients (6.5 %) developed contact dermatitis [23].

3.7. St. John’s Wort (Hypericum perforatum (L.))

Psoriatic keratinocytes show increased cell proliferation, disturbed cell differentiation, an inflammatory phenotype and reduced expression of cationic channels such as TRPC6. Hyperforin—the major lipophilic active ingredient of St. John's wort—displays in vitro pronounced anti-inflammatory effects and stimulates calcium influx into psoriasis keratinocytes, activates TRPC6 expression, reduces cell proliferation and promotes proper cell differentiation [24].

4. Wound healing

Wound healing is a natural physiological response to tissue injury and involves a complex interplay between numerous cell types (keratinocytes, fibroblasts and immune cells), cytokines and the vascular system to stop bleeding, kill bacteria and initiate re-epithelialization. Most herbal remedies traditionally used for wound healing have not been investigated in controlled clinical studies [25]. In contrast, the wound-healing properties of a betulin rich extract from the bark of white birches have been thoroughly investigated. This extract allows the production of a solid phase stabilized emulsion without conventional emulsifiers or preservatives [26]and will be described in more detail.

4.1 Birch bark (*Betula* spp.)

The wound healing properties of betulin have been elucidated at the molecular level and positively affects all 3 phases of wound healing (inflammatory phase as well as migration and differentiation phase of keratinocytes) [27]. First clinical evidence for the wound healing properties of betulin were achieved in a split thickness wound study with topical application of a water free betulin oleogel [28].

4.2 Onion *(Allium cepa* L.*)*

A systematic review published in 2017 on anti-scarring agents mentions many positive outcomes in scarring management with onion extract [29].

5. Conclusion

Botanical compounds such as salicylic acid, methoxsalen and chrysarobin have been traditionally used and still play an important role in the treatment of psoriasis. Recently, the alkaloid indirubin from indigo has been shown to be effective in psoriasis in randomized clinical trials. Glycyrrhetinic acid and licochalcone A from licorice have been shown to be effective in the treatment of atopic dermatitis. Only recently, betulin-oleogel obtained from birch bark has been approved as a drug for the topical treatment of superficial wounds and burns. These examples illustrate that botanical compounds and extracts have a great potential to be developed as prescription or over the counter drugs in dermatology.

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