Abstract

Cardiospermum halicacabum is a tropical plant with interesting potential, making it a strong candidate to become a useful remedy in treating local dermatitis. Nowadays, inflammatory diseases of the skin are having increasingly serious implications: global incidence is more and more widespread and is, unfortunately, increasing. The problem of atopic syndromes is a clear example. The main pharmacological treatments prescribed in medicine foresee the use of cortisone and antihistamine preparations. These therapies, if applied to large areas of the skin and for prolonged periods, can cause adverse reactions, including on a systemic level, which may also occur when these drugs are administered orally. That is why it is important to evaluate the efficacy of natural remedies, such as Cardiospermum halicacabum, which, thanks to its components, is able to control the problem of dermatitis without causing the relative collateral effects, even at paediatric level.

THE SKIN

The skin, this large involucrum that encloses the entire body, is the most important intermediary between us and the external world. The skin acts as a barrier against pathogenic microorganisms, as well as against environmental pollution; it protects the internal organs from sudden changes in temperature and it has perfectly organized defence mechanisms.

In an adult, the skin, on average, has a surface area of 2 m² and can weigh from 3-5 kg. It is certainly the organ that is most often exposed to the risk of trauma, infection and disease and is constantly stressed and conditioned by exposure to solar radiation. (1)

It is evident that if cutaneous homeostasis should be somehow compromised, the protective functions of the skin could be modified and decreased; thus triggering an inflammatory effect, classified as dermatitis, which with all the correlated symptoms can lead to staphylococcal and streptococcal infections, but also fungi and viruses. (2)

Traditional pharmacological therapy, normally with the aim of opposing the dermatitis clinical picture, is generally based on cortisone or antihistamine drugs, either via topical or general use; in most cases this approach is efficacious, but has some adverse reactions. Moreover, the problem of dermatitis, due to its relapsing nature, needs prolonged medical care, therefore, the long term prescription of cortisone drugs should be carefully considered. Even if application is limited to local use, these drugs can cause the same adverse reactions as detected after systemic therapy: in certain types of atopic dermatitis the areas of cutaneous application are so extensive that the absorption of the active principles can be significant enough to induce important systemic effects, especially and dangerously in the paediatric domain. (3)

For these reasons, evaluating the possibility of using a remedy of natural origin, allowing the problem of dermatitis to be faced in an efficacious and safe way and for prolonged periods, is an ethical choice.

THE PLANT AND ITS CONSTITUENTS

The phytotherapeutic approach to dermatitis can benefit from the properties of an exotic plant native to India and widely...
used in Ayurveda: Cardiospermum halicacabum, which belongs to the Sapindaceae family. The name “cardiospermum” derives from the peculiar appearance of the seeds, which are black, with a light heart-shaped spot. The term “halicacabum” comes from the Greek for salt-cellar, alluding to the shape of the capsule that contains the seeds.

In the Tamil language, Cardiospermum halicacabum is called “Modakathon”, which means “remedy for debilitating pain”, underlining the use that traditional Indian medicine has been making of this plant for centuries: the treatment of acute and chronic inflammatory rheumatism.

Picture 1. Cardiospermum halicacabum.

The characteristics of the Cardiospermum halicacabum phytocomplex highlight a series of components that are strong candidates in expressing a significant anti-inflammatory action, even at cutaneous level. The main active components of the plant are extracted from the flowering aerial parts. They include a substantial group of saponins such as glycocidal triterpenes (4), hydrolysable tannins (5), traces of alkaloids, quebrachitol, a particular alcohol with a base structure that can be traced to that of inositol, several flavonoids, amongst which apigenin and luteolin, pentacyclic triterpenes (6), and especially plant sterols, such as beta-sitosterol, stigmasterol (7,8,9,10,11,12).

Oil is extracted from the seeds (33%) and contains a significant quantity of cyanolipids (13-55%). These rare compounds are divided into 4 groups, all different, but all made of a base structure of long chain fatty acids esterified with a hydroxy isoprenoid or dihydroxy-nitrile group.

The most commonly used pharmaceutical preparations in modern phytotherapy only refer to the green and flowery components of the aerial parts and not to the seeds. The components of Cardiospermum seem to express their anti-inflammatory action with a cortisone-like mechanism, in particular by modulating the activation of phospholipase A2 while maintaining the stability of cell membranes. This effect is due to the presence of phytosterols, which are known to be structurally similar to cholesterol and, for this reason, present a certain affinity for lipids in the epidermis and cell membranes. Phytosterols also perform a homeostatic cutaneous and anti-aging action.

According to several authors, phytosterols could stimulate fibroblast activity, thus promoting granulation of damaged areas and tissue to repair the typical damage caused by scratching which is so frequent in the case of dermatitis. Moreover, the cortisone-like action of the phytosterols allows for good control of pruritus symptoms, an activity which is potentiated by the presence of tannins in the Cardiospermum phytocomplex, known to have an astringent and haemostatic effect when applied locally. Additionally tannins are able to inhibit hyaluronidases; an enzyme which takes part in the inflammatory process, since it degrades hyaluronic acid and at the same time promotes histamine release. (17)

The plant contains a good quantity of triterpene saponins, the local effects of which have not yet been clearly defined. Nevertheless, this category of substances has already shown important activity against inflammation; one significant example is that of liquorice flavonoids (12).

TESTING AND ACTIVITY

Thanks to the peculiar formulation of its phytocomplex, Cardiospermum halicacabum has been always appreciated by popular medicine for its analgesic and anti-inflammatory properties. These therapeutic indications raised strong interest in the academic world and nowadays have been evaluated and confirmed by several in vitro and in vivo studies. In the first studies done, results showed that the alcoholic extract of the aerial parts produces sedative and painkilling effects. When administrated via the intraperitoneal route in mice, it expressed a marked depressive effect on the Central Nervous System; once again, similar administration in mice demonstrated analgesic action in the heat radiation test. The analgesic and anti-inflammatory properties of Cardiospermum halicacabum have also been confirmed in the “granuloma pouch test” conducted on rats. It showed an action comparable to that of phenylbutazone (13) and the same result has been seen in the carrageenan-induced swelling test (14).

An interesting study conducted by Sadique and collaborators, compared the effects of Cardiospermum halicacabum to those of hydrocortisone for the control...
of artificially induced inflammation in laboratory animals. Also in this case the plant highlighted marked anti-inflammatory activity, although this was lower than the drug, the mechanism was similar to that of the steroid.

A multicentric observational study, in which 833 individuals, affected by various forms of dermatitis, including allergic dermatitis, were enrolled for four weeks, showed therapeutic efficacy in 80% of cases, with improvement and remission of typical symptoms.

The efficacy of Cardiospermum also appeared in lichenification, which characterize a chronic state of disease, in 72% of cases. Tolerability was good/very good in 87% of patients and was confirmed by unbiased examination by medical doctors.

Recent work done by M. S. Sheeba and V. V Asha and published in the Journal of Ethnopharmacology 124, 7-2009, confirms the anti-inflammatory and analgesic activity of Cardiospermum halicacabum and suggest additional mechanisms of action. In particular the study shows that the ethanolic extracts of the plant are able to significantly inhibit the expression of COX-2, TNF-α and iNOS, induced by stimulation with LPS rat cells, through modulation of NF-κB synthesis.

The study was conducted on RAW264.7 cells of the macrophage cell line of the mouse and also verified the possible toxicity of the extracts regarding the vitality of the cell culture: after 48 hrs of co-incubation, no toxicity effects were observed, even with increasing dosage of the extract.

The Sheeba and Asha test partially clarified the mechanism with which this phytocomplex explicates its already known analgesic and anti-inflammatory effects, but during the study other very interesting data came up, which confirm the great safety in the usage of this plant. As a matter of fact, contextually to the evaluation of concentrations of TNFa, COX-2, iNOS and NF-κB, the levels of COX-1 were also evaluated. These levels are normally inhibited by the activity of the well-known anti-inflammatory drugs, with serious consequences for the stability of the digestive system’s mucosa, nephritic functionality and the activity of platelets. After introduction into the cell culture of Cardiospermum halicacabum, these levels were not subjected to any decrease and were maintained at the same level as the control group [15].

These results are confirmed by an additional study conducted by P. Pratheeshkumar and Girija Kuttan, published in the Asian Pacific Journal of Cancer Prevention vol. II, 2010, where the methanolic extract of Cardiospermum halicacabum, opposed the immunosuppressive effects and oxidative stress induced by cyclophosphamide (CTX). This chemotherapeutic drug is known to produce myelosuppression, as highlighted by a decreased WBC count. Co-treatment with Cardiospermum countered these onsets, increased the relative organ weights of spleen, as well as thymus, when compared to the group treated with just CTX. Cardiospermum also significantly increased the glutathione (GSH) levels in animals treated with CTX, while highlighting antioxidant properties and further reducing the enhanced levels of pro-inflammatory cytokines like TNF-α, IFN-γ and IL-2. [16]

CONCLUSIONS

The collection of these data leads to Cardiospermum halicacabum being considered as a plant with interesting potentiality of action in many forms of skin inflammation. In particular, the safety of use suggests indication in many forms of dermatitis in paediatrics, in adults and in the elderly. The plant has indications in atopic dermatitis, in contact dermatitis, in keratosis and in lichenification, where, thanks to the anti-inflammatory and skin-loving activity of its components is succeeds in re-establishing cutaneous homeostasis while calming important symptoms such as pruritus.

It can also be useful in the treatment of seborrhoeic dermatitis, cradle cap in babies and the increasingly frequent sun-rashes, where it mimics cortisone activity but without producing phenomena of photosensitization.

The data on safety of use, at the current stage of research, candidate the Cardiospermum halicacabum extracts as one of the first choice topical anti-inflammatory treatments, even for the most serious and relapsing forms. The selective action of the plant towards anti-inflammatory mediators prevents the final user from experiencing consequences linked to the systemic effects that are potentially consequent to extensive and prolonged use of preparations for local treatment.
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The real needs of people can’t be found in a laboratory. That’s why we get our inspiration where these needs can be found — in real life.

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