Asthma, *Euphorbia hirta* and its anti-inflammatory properties

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**Euphorbia hirta** is a plant used in traditional medicine for a variety of diseases, such as cough, asthma, colic dysentery and genito-urinary infection. This plant, belonging to the family *Euphorbiaceae*, is also known as the Australian asthma herb or Queensland asthma weed, and is not toxic when taken in typical dosages. In South Africa, it is commonly used for asthma, which is one of the most common respiratory complaints. Although corticosteroids are considered the best means of defence against this debilitating illness, many people, especially in poor countries, rely on herbal remedies for its treatment. We discuss recently published results to assess the effect of the plant using the BALB/c murine asthma model. We also review the different compounds found in plant extracts, in an attempt to understand the reason for its anti-inflammatory properties. We conclude that the flavonoids quercitrin (converted to quercetin in the alimentary canal) and myricitrin, as well as the sterols 24-methylene-cycloartenol and -sitosterol, exert noteworthy and dose-dependent anti-inflammatory activity. The triterpene β-amyrin also seems to exert a similar anti-inflammatory activity. Tannins and tannic acid derivatives, also present in the plant, have antiseptic effects and the two triterpenoids, taxerone (EH-1) and 11α, 12α-oxidotaraxerol (EH-2), in *E. hirta* demonstrate antibacterial and anti-fungal properties. The effectiveness of *E. hirta* in treating asthma may lie predominantly in the synergistic relationships between the flavonoids, sterols and triterpenoids.

**Introduction**

Asthma is one of the most common respiratory complaints in the world today. It affects an estimated 300 million people worldwide, of whom about 50 million live in Africa, 15 million in the U.S., 5 million in the U.K. and 2 million in Australia. Ten per cent of asthma sufferers are children and 5% are adults. Asthma mortality in the United States amounted to some 5000 persons in the year 2000. The global prevalence of the disease is expected to rise to 400 million by the year 2025. Most of the available pharmacological therapies simply control the known mechanisms by which the disease occurs. There is no complete cure for asthma. Pharmaceutical products have been the main source of anti-asthma treatment but some of these have recently been associated with serious adverse effects.

It is estimated that there are about 27 million consumers of indigenous medicine in southern Africa, a large number of whom consult traditional healers for potentially life-threatening conditions. An estimated 60% of the South African population is reported to consult traditional healers. Moreover, the steady increase in incidence of asthma has, as with any chronic condition, opened up a new era where sufferers are resorting to alternative treatments.

One of the herbs used against asthma in southern Africa is *Euphorbia hirta* (family *Euphorbiaceae*), also known as the Australian asthma herb or Queensland asthma weed, cat’s hair, hairy spurge, spurge or milkweed. In India, the plant is used for...
treating a variety of diseases, such as cough, asthma, colic dysentery and genito-urinary conditions. In East and West Africa, extracts of the decoction of the flowering and fruiting plants are used in the treatment of asthma and respiratory tract infections and are sometimes in the treatment of asthma and respiratory tract infections and are sometimes.

The BALB/c murine asthma model was used to investigate the consequences for mice exposed to low-dose hydrocortisone (HC) (100 mg/kg), mice exposed to higher-dose HC (125 mg/kg), and mice subjected to physiologically comparable levels of E. hirta (0.01 ml of 62.5 mg/kg plant material).

White blood cell counts are a reliable measure of asthmatic status. The process of inflammation in asthma is viewed as an inflammatory cascade, which is divisible into seven phases: sensitization, stimulation, cell signalling, migration, cell activation, tissue stimulation or damage, and resolution. In humans, eosinophil numbers are elevated in the airways of asthmatics and these cells release basic proteins and growth factors that may damage airway epithelial cells, and cause airway remodelling. Additionally, neutrophil population is usually found to increase in the airways and in sputum of patients with severe asthma. It is therefore useful to examine these counts, to determine if an anti-asthmatic product is effective, particularly when compared with results from exposure to hydrocortisone (which, in our case, was used as a positive control) and reduces white blood counts in asthma. Table 1 shows that the mice in the asthmatic group (made asthmatic and not treated with any product) met the criteria for an asthmatic state. Both doses of hydrocortisone lowered the white blood counts in the mice, as did the plant extract. The neutrophils, eosinophils and basophils specifically were also lowered; these cells are known to be active in inflammation.

Platelets and fibrin networks also play a fundamental role in asthma. Pretorius and co-workers showed that control mice possess major thick fibres and minor thin fibres as well as tight round platelet aggregates with typical pseudopodia formation. Minor fibres of asthmatic mice have a net-like appearance, covering the major fibres, whereas platelets appear to form loosely connected, granular aggregates. Both concentrations of hydrocortisone made the fibrin more fragile, and platelet morphology changed from a tight platelet aggregate to a more granular assembly, not closely fused to one another. Furthermore, it was claimed in the article that E. hirta does not influence the fragility of the fibrin and that it prevents the minor fibres forming the dense net-like layer over the major fibres, as is observed in untreated asthmatic mice. Furthermore, it seems that E. hirta does not render the fibrin fibres as fragile as is found with the HC-treated mice and it also does not alter the integrity and morphology of the platelets as was found in HC-treated mice. An important result is that E. hirta reduces inflammatory cells to the same level as that achieved by hydrocortisone, suggesting that the plant, indeed, has anti-inflammatory properties.

The question that now arose is, what components give the plant these properties? A review of the relevant available literature now follows.

### Chemical compounds of Euphorbia hirta

Phytochemical analyses of E. hirta reveal flavonoids, sterols, tannins and triterpenoids in the bark and leaves.

#### Flavonoids

Two flavonoids have been isolated from E. hirta, namely quercitrin and myricitrin.

In general, flavonoids have been reported to possess several proven medicinal properties including anti-inflammatory, antioxidant, anti-allergic, antibacterial and antiviral activity. The most abundant flavonoid in E. hirta is quercetin, which has been reported to be the main agent that addresses the inflammatory component of asthma. Flavonoids have been proposed to exert beneficial effects in many diseases, including asthma. Many of the biological actions of flavonoids have been attributed to their antioxidant properties, either through their reducing capacities or as a result of their possible influence on intracellular redox status. Flavonoids can also interact selectively within the mitogen-activated protein (MAP) kinase signalling pathway.

### Possible anti-asthmatic effects of quercetin

Quercetin (3-rhamnose-3-rhamnose), found in E. hirta, is a bioflavonoid with antioxidant and anti-inflammatory properties. It is converted in the alimentary canal to quercitin (3-O-β-L-rhamnopyranoside), which is the aglycone product of the former. It is this converted product, quercitin, that is a potent anti-inflammatory chemical, and is believed to be the most important constituent in the plant responsible for the anti-asthmatic effects.

#### Sterols

Sterols that have been isolated from E. hirta and have been chemically characterized include cycloartenol, 24-methylene-cycloartenol, β-sitosterol, euphorbol hexacontenate, 1-hexacosanol, tinaloxin, campesterol and stigmasterol. The compounds 24-methylene-cycloartenol and β-sitosterol have also been found to exert significant and dose-dependent anti-inflammatory effects, when treating acetate-induced ear inflammation.

#### Tannins and triterpenoids

Tannins are not widely known for their anti-inflammatory potential; E. hirta possesses a few such chemicals. Phytochemicals work synergistically, however, and therefore these tannins may assist in the anti-inflammatory action of the plant. Euphorbia hirta presents three hydrolysable tannins, namely, dimeric hydrolysable tannin, euphorbin E and the dimeric dehydroellagitannins, euphorbin A and euphorbin B. Chen also isolated the following tannins from the leaves of E. hirta, using physicochemical and spectroscopic methods: gallic acid, 2,4, 6-tri-O-galloyl-D-glucose and 1,2,3,4, with the criteria for an asthmatic state.

<table>
<thead>
<tr>
<th>Control group</th>
<th>Asthma group</th>
<th>Low HC (100 mg/kg)</th>
<th>High HC (125 mg/kg)</th>
<th>E. hirta (0.01 ml of 62.5 mg/kg plant material)</th>
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<tbody>
<tr>
<td>Neutrophil</td>
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<td>91</td>
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<td>2</td>
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<td>1203</td>
<td>41</td>
<td>81</td>
</tr>
<tr>
<td>Monocyte</td>
<td>203</td>
<td>737</td>
<td>32</td>
<td>63</td>
</tr>
</tbody>
</table>

Table 1. Summary of mean white blood cell counts in blood smears obtained from control group, asthmatic mice, asthmatic mice treated with low and high hydrocortisone (HC) doses, as well as asthmatic mice treated with Euphorbia hirta (5 areas from each blood smear, and 5 smears from each individual mouse, were counted; there were 6 mice per group).
6-penta-O-galloyl-β-D-glucose as well as the quinic acid ester, 3,4-di-O-galloylquinic acid. 39

Research has shown that triterpenoids possess anti-inflammatory properties. The triterpenes α-amyrin, β-amyrin, taraxerone (EH-1), taxerol as well as 3,4-di-O-galloylquinic acid, gallic acid, ellagic acid, terchebin. 34


d Table 2. Chemical compounds isolated from Euphorbia hirta. 

| Flavonoids (flavonol glycosides) | Quercitrin, isoquercitrin, myricitin |
| Tannins | Dehydrodihlittannins, eurphorin A, eurphorin B (isomer of eurphorin A), eurphorin E, Galloyl/galloyl, 2,4,6-tri-O-galloyl-glucose, 1,3,4,6-tetra-O-galloyl-glucose, 1,2,3,4,6-penta-O-galloyl-D-glucose, geramin, 4,5-D-cafeoylquinic acid, 3,4-di-O-galloylquinic acid, gallic acid, ellagic acid, terchebin. |
| Triterpenoids | α-Amyrin, α-amyrin, β-amyrin acetate |
| Sterols | Taraxerol (EH-1), taxerol, 11α; 12α-oxidotaraxerol (EH-2) |
| Cycloartenol (precursor in photosynthetic organisms), β-sitosterol, campesterol, stigmasterol, cycloartenol, 24-methylene-cycloartenol, euphorbal hexacosonate |

6-penta-O-galloyl-β-D-glucose as well as the quinic acid ester, 3,4-di-O-galloylquinic acid. 39

Research has shown that triterpenoids possess anti-inflammatory properties. The triterpenes α-amyrin, β-amyrin, taraxerone (EH-1), taxerol as well as 3,4-di-O-galloylquinic acid, gallic acid, ellagic acid, terchebin. 34 These compounds induce both antibacterial and antifungal properties, as well as tested against fourteen pathogenic bacteria and six fungi.

**Anti-inflammatory action of E. hirta**

Table 2 shows the various components with anti-inflammatory properties that have been isolated from *E. hirta* thus far. Despite this variety of chemical compounds and the diverse local medicinal uses of the plant, it appears as if the flavonoids quercitin and myricitin are the compounds that induce the anti-inflammatory effect. However, the sterols, 24-methylene-cycloartenol and β-sitosterol, 36 and the triterpene, β-amyrin, also seem to display anti-inflammatory properties. Furthermore, tannins and tannic acid derivatives have antiseptic effects and the two triterpenoids, taraxerone and 11α, 12α-oxidotaraxerol, in *E. hirta*, also display antibacterial and antifungal properties.

These compounds in combination may have a synergistic effect, and may be the reason why *E. hirta*, as herbal medicine, has its claimed efficacy.

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