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Fumaric acid esters

What are fumaric acid esters?

The fumaric acid esters (FAE) monoethylfumarate (MEF) and dimethylfumarate (DMF) are chemical compounds derived from the base compound fumaric acid. Fumaric acid is a food additive commonly found in sweets and cakes. In this chemical state, fumaric acid is poorly absorbed and passes straight through the body without causing any effects. On the other hand, fumaric acid esters are potent chemicals or drugs that have been used to treat [psoriasis](#) for over 30 years. However, it is only within the last decade that serious clinical research has been carried out to determine their use, effectiveness and safety in the treatment of psoriasis and other skin conditions.

It is important to emphasise the difference between fumaric acid and fumaric acid esters. Fumaric acid formulations are available as health supplements and often marketed as a natural alternative medicine to treat psoriasis. They are in fact poorly absorbed by the gut and basically excreted via urine without having any therapeutic effect whatsoever.

What is the history of fumaric acid esters?

The use of fumaric acid esters in the treatment of psoriasis was first introduced in the late 1950's by the German chemist Schweckendiek. A standardised "fumaric acid" protocol for psoriasis was developed and used FAEs both orally and topically (ointment and bathing solution). Results were promising but there were associated serious side effects.

At that time it was thought that psoriasis was caused by a biochemical defect of the citric acid (Krebs) cycle, of which fumaric acid plays a role. Although the mode of action of FAEs and their place in psoriasis therapy remains unclear, evidence suggests that it has nothing to do with the Krebs cycle and the major active compound appears to be dimethylfumarate (DMF). This is thought to work by correcting the immunological imbalance that exists in psoriasis (shifting from a Th1 pattern of immune response to a Th2 one).

Who uses fumaric acid esters?

Fumaric acid esters have been used to treat severe psoriasis in northern Europe for over 20 years. However, the use of FAEs remains unregistered in most countries outside of Germany, including the UK, USA and NZ. Currently the only licensed FAE is the product Fumaderm, and is made up of dimethylfumarate and calcium, magnesium, and zinc salts of monoethyl hydrogen fumarate. This product has been approved for use in Germany since 1994. Other countries are seeking to licence the product but to date it remains unapproved by the FDA or Medsafe (New Zealand) for the treatment of any disease.

Many recent studies have shown that FAEs are an effective therapy in patients with severe psoriasis who have tried and failed conventional psoriasis treatments. Patients tolerating FAE therapy can expect a 75% improvement in their psoriasis in four months. In addition, FAEs are being used in combination with second line drugs such as [ciclosporin](#), [methotrexate](#) and [hydroxyurea](#) for additional benefit or to facilitate dose reduction of the second line agent.

What are the side effects of fumaric acid esters?

The main side effect that causes a high dropout rate in most clinical trials is gastrointestinal complaints, which

occur in up to 60% of patients. Gastrointestinal problems manifest as diarrhoea, nausea and stomach cramps and pains. In addition, flushing occurs in 30% of patients and is worse at the onset of therapy.

Other more serious side effects that have occurred include kidney disturbance and reduced function and white blood cell abnormality. It is essential that kidney function and blood count should be monitored regularly when taking FAEs. These changes appear to be reversible when treatment is stopped and to date there are no reports of severe long-term toxicity.

Further studies are required to determine how exactly FAEs work in psoriasis. Dimethylfumarate appears to be the major active ingredient and further investigation into refining the currently available FAE formulation may reduce the side effect profile and make it a more acceptable treatment for psoriasis.

Related information

References:

- Ormerod AD, Mrowietz U. Fumaric acid esters, their place in the treatment of psoriasis. Br J Dermatol 2004;150:630–632. [Medline](#).
- Harries MJ, Chalmers RJ, Griffiths CE. Fumaric acid esters for severe psoriasis: a retrospective review of 58 cases. Br J Dermatol 2005;153(3):549–51. [Medline](#).

On DermNet NZ:

- [Psoriasis](#)

Other websites:

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Author: Vanessa Ngan, staff writer

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