

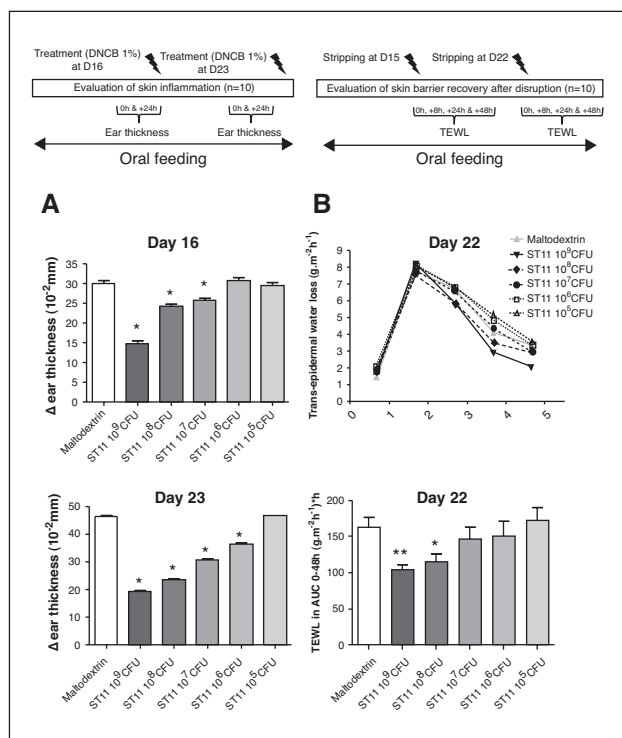


**Figure 1.** Effect of *Lactobacillus paracasei* CNCM I-2116 (ST11) on skin barrier function and skin inflammation: Dose-response study in mice. **A)** Experimental design: Ten mice in each group were fed by ST11 from D0 to D24 and recovery of skin barrier function was followed during 48 h after repeated tape stripping done at D15 and D22. Dose dependant effect of ST11 on ear thickness at day 16 and day 23. Data are represented by mean  $\pm$  SEM. \* $p < 0.001$ . **B)** Experimental design: Ten mice in each group were fed by ST11 from D0 to D23 and ear thickness was assessed 24 h after DNFB challenge at D16 and day 23. Top right panel: Kinetic of Trans-epidermal water loss at day 22. Results are expressed by mean  $\pm$  SEM. Down right panel: Area under curve (AUC) between 0 and 48 h. Results are expressed by mean  $\pm$  SEM. \* $p < 0.02$ ; \*\* $p < 0.01$ .

the basal TEWL value was  $1.81 \pm 0.07$  and reached a value of  $6.5 \pm 0.13$  just after tape stripping, offering a 3.59 ratio between them. At day 22, the basal value was similar to day 15, however, the ratio increased to 4.9 times (130% vs day 15), potentiating the possibility of ST11 to modulate the TEWL.

In the present study, oral supplementation with ST11 may be considered as a promising approach for treating subjects suffering from dry and inflamed skin. ■

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## Folic acid allergy: no breakfast cereal hazard

Folate is the generic term for a group of related B-vitamins acting as single-carbon-transfer co-enzymes. As deficiency is a cause of infant neural tube defects, and the daily reference intake of 400  $\mu$ g of folate equivalent is not easily achieved on an average diet, pharmaceutical folic acid (FA) preparations are available for substitution. Moreover, FA is added to a variety of convenience foods, and FA-fortification of cereal grain products is mandatory in some countries, including the US and Canada [1, 2].

Allergic anaphylaxis is a rare, but potentially dangerous side effect of FA-preparations [3-5]. Recently, an IgE-mediated mechanism could be demonstrated by IgE binding to folate-albumin [3]. Naturally occurring folates are tolerated by sensitised patients who are generally advised to avoid all artificially added FA [3-5]. Total abstinence however is getting increasingly difficult due to substitution in every day food. The question arises whether sensitised individuals are really at risk of developing anaphylaxis when consuming FA-fortified products.

We report a 45-year old woman who developed generalised urticaria and angioedema, accompanied by difficulty in swallowing 30 minutes after ingestion of a 5 mg FA-tablet. Intake of the same supplement had been well tolerated during a pregnancy some 10 years before. Her diet included vitamin-enriched products, such as ready-to-eat breakfast cereals. This was her first episode of hives.

Prick tests were performed using the FA-tablet, an intravenous FA-preparation, folinic acid (5-formyl-tetrahydrofolic acid), and tetrahydrofolic acid (THF). Intradermal tests were carried out using intravenous FA and folinic acid-preparation, diluted up to 1:1,000. While skin tests with folinic acid and THF were negative, prick and intradermal tests with FA were strongly and unequivocally positive. Three healthy volunteers showed no skin reactions with the FA-preparations. Graded oral provocation with FA up to a single dose of 400  $\mu$ g (the cumulative dose being 660  $\mu$ g) was well tolerated by our patient, defining an individual with no observed adverse

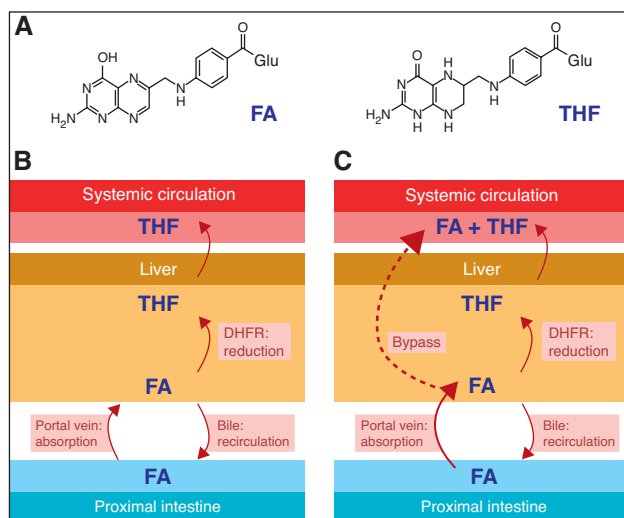


**Figure 1.** A) Folic acid (FA) represents the most oxidised form of folate with regard to its pteridine ring, whereas naturally occurring derivatives, e.g. tetrahydrofolic acid (THF), are reduced. Glu = Glutamate residue. B) Following ingestion of low doses, FA is completely reduced to THF by dihydrofolate reductase (DHFR). Additionally a considerable amount of FA is released into the bile entering enterohepatic recirculation. C) DHFR is saturated and bypassed following intake of high doses of FA, which may then reach systemic circulation in an unmetabolised form.

effect level (NOAEL). She denied further increment of provocation doses to establish the lowest observed adverse effect level (LOAEL). Her blood levels of folate, vitamin B12, and a full blood count were normal.

Tolerance of low FA doses is supported by documentation of reactions provoked following intake of several hundred  $\mu\text{g}$  [4], while there are no reported episodes of anaphylaxis due to ingestion of FA-fortified foods. Synthetic FA, correctly referred to as pteroylmonoglutamic acid, does not occur naturally. It represents the most oxidised form of folate. Skin tests with naturally occurring, reduced folates (THF and 5-formyltetrahydrofolic acid) were negative in our patient. This is consistent with most reports [4], though different patterns of skin test cross-reactivity have been described [3].

Upon ingestion, FA is absorbed in the intestine and transferred to the liver via the portal vein (figure 1). A considerable amount is released into the bile, entering enterohepatic recirculation. Generally, FA is reduced by dihydrofolate reductase (DHFR) [2, 6] thereby becoming indistinguishable from natural folates that are stored in the liver as polyglutamates and may be released to systemic circulation, linked to folate binding proteins. Upon intake of high doses of FA, DHFR may become saturated and bypassed by unmetabolised FA. We hypothesise that high doses of FA lead to significant amounts of unreduced FA circulating, which produces the anaphylaxis-triggering allergen. Our patient's NOAEL of 660  $\mu\text{g}$  exceeds the daily reference intake of 400  $\mu\text{g}$  and is hardly achievable by the consumption of a single FA-fortified meal. However, DHFR activity significantly differs among patients [6] resulting in an individual NOAEL which might be as low as 110  $\mu\text{g}$  [5]. Our findings underline the need for an individualised allergological work-up, not only to establish FA-allergy

diagnosis but also to enable detailed recommendations, preventing unnecessary dietary restrictions. ■

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## Simple new operative technique to treat ingrown toenails without recurrence

Ingrown toenail is a relatively common foot problem. Many surgical treatment modalities have been described. Surgical approaches include partial nail avulsion or complete nail excision, with or without matricectomy. Herein we present a simple and minimally invasive surgical approach without nail avulsion or excision and matricectomy.

One hundred and five patients with stage 2 and 3 ingrown toenails admitted to the general surgery clinic between January 2007 and December 2009 were included in the study. Seventy-four patients, (41 men, 33 women, mean age 26.3 years), operated on by the same surgeon, were considered as surgical treatment group (ST). The remaining thirty-one patients who refused surgery were treated with conservative non-surgical therapy. These patients were considered as the non-surgical therapy group (NST). In the ST group, short term results were excellent with only minimal discomfort and pain. The cosmetic appearance was favourable. A natural outcome was achieved by preserving of nail plate, nail bed and matrix. Mean postoperative follow-up was 26.4 months (range 6-42 months). No major complications were detected in this series during the study period. There was no recurrence during the follow-up