

- (3) The authors claim that CF cells are unable to transport GSH adducts, which overstates the case, otherwise standard CF therapies would be toxic to CF persons. For example, MRP channels have been identified at the basolateral side of human lung epithelial cells, which channels function even in CF.
- (4) According to the most recent peer-reviewed literature, the primary selection force for CF mutation was the bubonic plague epidemic of the 1300–1500s. Not lead, not cholera.
- (5) Abnormal zinc levels have a role to play in the explanation of CF pathology. Some CF children do present with severe zinc deficiency, but this is due to malabsorption. When pancreatic enzymes are introduced and/or oral zinc supplementation given, the deficiency can be normalized in plasma and in cells (see, for example, [4–6]).

The authors imply that exogenous supply of isothiocyanates can ameliorate CF. Not only are there potential questions of toxicity (besides SCN toxicity, should we be diminishing even further the deficient leukocyte levels of GSH in CF, given Tirouvanziam's findings?), it is difficult to overstate how little justification is provided by the manuscript for such a leap.

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Potential therapeutical effects of cannabidiol in children with pharmaco-resistant epilepsy

Dear Editor,

Over the last few years considerable attention has focused on cannabidiol (CBD), a major non-psychoactive constituent of *Cannabis Sativa*, which is currently investigated as a therapeutic option in the treatment of some psychiatric disease such as anxiety disorders and schizophrenia [1]. Although the anticonvulsive properties of CBD have been known since the early eighties [2], only a few recent papers have addressed its use in samples affected with epileptic disorders. The major reasons for the lack of clinical research have been the introduction of new synthetic and more stable pharmaceutical anticonvulsants, the recognition of important adverse effects and the legal restriction to the use of cannabis-derived medicines [1].

Working from these assumptions, we hypothesize that nowadays CBD can be tested as monotherapy in children with a severe epilepsy refractory to conventional antiepileptic agents. There are at least five lines of evidence supporting this hypothesis. First, molecular advances have shown that CB1 receptors are present in two very different neuronal subpopulations (i.e. inhibitory GABAergic neurons and excitatory glutamatergic neurons), and that CB1 receptor agonists (as Δ^9 THC) have been shown to be both pro- or anti-convulsive [3]. However, CBD has been shown to exert its effects through a mechanism that does not involve CB1 receptors and without increasing neuronal excitability [4]. Second, as many anticonvulsants, CBD has some mood stabilizing properties and could be used in bipolar disorders [5]. Third,

recent therapeutic applications of CBD in adolescents suffering from neurodegenerative disease, mitochondriopathy, posthypoxic state, posttraumatic reaction, support its safety use in paediatrics [6]. Fourth, tolerance to the anticonvulsant properties of CBD is not a prominent feature and this may play a central role in subjects who have been previously treated with high-dose of anticonvulsants or with a combination of them. Fifth, nowadays CBD can be easily delivered by metered dose pump action aerosol spray, a delivery system particularly useful in children with a poor compliance [3].

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Thiazolidinediones as potential therapeutic agents in atopic eczema

Sir,

Current knowledge about the etiopathogenesis of atopic eczema (AE) has stimulated drug development focused on agents with less toxicity than current topical and systemic corticosteroids [1]. At this regard, recent molecular data have clearly shown that AE seems to be characterized by an increased expression of the water channel aquaporin 3 (AQP3) in skin biopsies [2]. Accordingly, Olsson et al. have demonstrated by means of DNA microarray analysis and real-time polymerase chain reaction that AQP3 is highly upregulated in the lesional epidermis of AE patients [2].

These findings may logically lead to the hypothesis that suppression of AQP3 expression in AE skin could represent a novel therapeutic target in the management of this allergic dermatosis. Specifically, we speculate that thiazolidinediones (TZDs), a class of agents currently used for the treatment of type 2 diabetes mellitus, may be also of potential therapeutic benefit in the treatment of AE lesions. TZDs may indeed promote a significant suppression of AQP3 expression, at both the mRNA and protein level [3,4], probably

by modulation of the AKT/mTOR/p70(S6K) signalling pathway [3].

Given that topical preparations of TZDs are currently being developed [5] – and that local administration with TZDs has been already tested successfully in several animal models [5,6] – we believe that future human studies investigating the potential efficacy of TZDs in AE patients will be of great interest for testing our hypothesis.

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