Unsaturated fatty acids esterified with androgens as active and safer compounds for androgen-required therapy

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Testosterone and its powerful metabolite dihydrotestosterone can be used in a variety of disorders to improve the symptoms or restore androgen plasma levels. To increase their duration and effects, androgens are administered in different pharmaceutical forms, in particular as esters of carboxylic acids.
The goal of our research was to use specific unsaturated fatty acids esterified with androgens to improve the pharmaceutical characteristics of the esters as well as their biological effects and safety. Oleic acid, linoleic acid and the n-3 fatty acids, alpha-linolenic acid, eicosapentaenoic acid and docosahexaenoic acid, were esterified with androgens. Their cytotoxicity was evaluated in mouse NIH3T3 and human astrocyte cell lines. The esters showed good tolerability and no *in vitro* cytotoxic effects in both cell cultures.
Due to the influence of androgens in pain processes and the common opioid-induced hypogonadism, *in vivo* studies were carried out to investigate their long-term administration in a pain model of persistent pain.
Androgen therapy can also be required in neurodegenerative disorders, for instance in X-linked adrenoleukodystrophy, an inherited pathology. Lipid alterations are the major cause of the disorder and hypogonadism can be a secondary event. In this specific disorder and in chronic pathologies with unbalanced lipid and steroid hormone metabolism, the use of the described esters, which are more “physiological” than the ones currently available, should be carefully considered.