

Letter to the Editor

D-Chiro-Inositol's action as aromatase inhibitor: rationale and potential clinical targets

Dear Editor,

D-Chiro-Inositol (DCI) is one of nine stereoisomers of inositol, a six-carbon polyalcohol¹. Inositol phosphoglycans play a key role in signal transduction of insulin and orchestrate hormonal regulation and oocyte developmental competence at ovarian level². In this scenario, a recent *in vitro* study found that DCI acts directly on steroidogenic enzymes gene regulation of human granulosa cells, reducing mRNA expression of both aromatase CYP19A1 and cytochrome P450 side-chain cleavage (P450_{scc}) genes in a dose-response manner in mature granulosa-lutein cells³. This action of DCI as aromatase inhibitor (AI) can be considered in line with the observation of a detrimental effects on blastocyst quality in case of high levels of DCI in the follicular fluid (FF)⁴: in particular, the best oocyte quality correlated with a MI:DCI ratio 70-100:1 in FF, whereas the 40:1 ratio administered by oral route has been found to reverse histological and functional features of PCOS in a mouse model⁵, and has been later confirmed as the best strategy for PCOS therapy in humans⁶. Considering its action as AI, we take the opportunity to speculate that DCI at high levels may be considered as a potential therapeutic/adjuvant strategy in clinical conditions in which the reduction of estrogens is the key target, such as endometriosis⁷ and estrogen-dependent breast and endometrial cancers⁸. In addition, high levels of DCI may be used alone or in combination with other AIs, such as letrozole, for ovulation induction, especially in the PCOS population⁹. Finally, since aromatase converts testosterone to estradiol, the inhibition of this enzyme by high levels of DCI can lead to increased (non-converted) levels of circulating androgens, which may play a beneficial role in several conditions, such as sexual dysfunction¹⁰ and for prevention of osteoporosis in both men and women.

Conflict of interest

Vittorio Unfer is an employee at Lo.Li. Pharma s.r.l., Rome, Italy. Antonio Simone Laganà has no proprietary, financial, professional or other personal interest of any nature in any product, service or company.

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