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Nomegestrol acetate: A possible candidate for endometrial cancer amelioration

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Endometrial cancer (EC) has been one of most common gynecological malignancies in western countries, and in China as well. Hysterectomy is a primary treatment but not suitable for patients who desire to preserve fertility and with advanced or recurrent disease. Several clinically used progestins showed different response rates for patients with different pathological types and stages and varied greatly (11-56%), especially in recurrent or advanced patients. Here, we investigated the inhibitory effect of several progestins, including nomegestrol acetate (NOMAC), medroxyprogesterone acetate (MPA), levonorgestrel, cyproterone and drospirenone on various types of EC cells. NOMAC, a highly selective 19-nor progestogen derivative, equally suppressed the growth of RL95-2, Hec1A and AN3CA cells and showed stronger activity than the other progestins in Hec 1A cells. *in vivo*, NOMAC decreased the growth of ectopic endometria in a rat model and produced a stronger inhibition on the growth of xenograft tumor of nude mice borne RL95-2 cell lines than MPA did, and the inhibition rates for 50,100, and 200 mg/kg NOMAC were 24.74%, 47.04% and 58.06%, respectively, and for 100 and 200 mg/kg MPA were 41.06% and 27.01%, respectively. When equal dose of NOMAC and metformin were combined (100mg/kg, respectively), the tumor volume inhibitory rate were increased by approximately 8% and 10% compared with metformin used alone in Hec1A and RL95-2 cells, respectively. Additionally, NOMAC induced apoptosis of RL95-2 and Hec 1A EC cells and arrested cell cycle at phase of Go/G1 and impeded the protein expression and the activity of mTOR and its downstream genes, such as 4EBP1 and eIF4G, but not influence the activity of Akt. Furthermore, when combining NOMAC and metformin, the activities of mTOR, 4EBP1 and eIF4G were more strongly suppressed, comparing with metformin used alone in Hec1A and RL95-2 cells. It suggests that NOMAC may have a potential ability against the growth of EC, which effect may associate with suppressing mTOR signaling, and metformin could enhance the effect in some degree.

Recent Publications

1. Zhang J F, Zhu Y, et al., (2014) Evaluation of biodegradable microspheres containing nomegestrol acetate in a rat model of endometriosis. Eur J Pharm Sci. 65:15-20.
2. Huang Q B, et al., (2014) Pharmacokinetics, tissue distribution and excretion of nomegestrol acetate in female rats. Eur J Drug Metab Pharmacokinet. 40(4):435-42.
3. He-Lin Lu, et al., (2014) An improved synthesis of nomegestrol acetate. Org. Process Res. Dev. 18(3):431-436.
4. Zhong R, et al., (2016) Kuntai capsule inhibited endometriosis via inducing apoptosis in a rat model. Evid Based Complement Alternat Med. 2016: 5649169.
5. Zhu Y, et al., (2015) Ginsenoside Rh2 suppresses growth of uterine leiomyoma *in vitro* and *in vivo* and may regulate ERα/c-Src/p38 MAPK activity. J Funct Foods. 18:73-82.

Biography

Yan Zhu has her expertise in pre-clinically reproductive pharmacology research and devoted to improve application of contraceptives for ameliorating gynecological diseases. She has received her PhD degree at Fudan University, China and studied as a Visiting Scholar at University of British Columbia, Canada. She is the PI of Lab of Reproductive Pharmacology and National Health Commission Key Lab of Reproduction Regulation, Shanghai Institute of Planned Parenthood Research, and she is the current Council Member of Chinese Pharmacological Society and the Director of the professional committee of Reproductive Pharmacology. She has published more than 90 scientific papers in Chinese journals and international journals indexed by SCI. She has received several grants from Shanghai Municipal Science and Technology Commission, and two of research projects were awarded 3rd prize by the Nation National Health Commission of China.

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