RESEARCH PAPER

Asian Journal of Bio Science, Vol. 4 Issue 2 : 162-165 (October, 2009 to March, 2010)

Evaluation of antiprogestin activity of a progesterone analog 14 - hydroxy progesterone in albino rats (*Rattus norvegicus albinus*)

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(Accepted : May, 2009)

Progesterone is important for initiation and maintenance of pregnancy (hormone of pregnancy).The discovery that in the absence of progesterone, pregnancy cannot be initiated or maintained provided the basis for a massive effort of synthesis of antiprogestin molecules to develop emergency contraceptive pills. By the consequences, till date few progesterone antagonists (antiprogestins) have been synthesized which bind to and block the progesterone receptor. However, none of the antiprogestins are "pure" antiprogestins, having marked antiglucocorticoid properties as well, especially at higher doses. Thus the search for the "ideal" progesterone antagonist continues. The main objective of the present work is to evaluate antiprogestin activity of progesterone analogue, 14 β- hydroxy progesterone. A pregnane glycoside, carumbelloside-I (3-O-beta-D-glucopyranosyl-(1→6)-beta-D-glucopyranosyl-3beta,14beta-dihydroxypregn-5-en-20-one) was isolated from the n-butanolic extract of Caralluma umbellata (Asclepiadaceae) and was modified to a structural analog of progesterone, 14 β- Hydroxy progesterone (14β- OHP) in just two simple steps. Anti-implantation and abortifacient activities of the compound have been studied to evaluate its antiprogestin activity. To study the anti-implantation effect, pregnant wistar strain albino rats were administered with 14β-OHP (daily dose of 5 mg/Kg body weight) intraperitoneally from the day 1 to day 7 of pregnancy. On day 10, laparotomy was performed under light ether anesthesia. The uteri were examined to determine the number of implantation sites. The abdomens were sutured and the animals were allowed to go on term. The number of young born at term was also recorded. The abortifacient activity was studied in another group of pregnant rats. The animals were treated with 14β- OHP (5 mg/Kg body weight daily) intraperitoneally from day 8 to 12 of pregnancy. They were sacrificed on day 19 of pregnancy. Both horns of uterus were observed for the number of live fetuses. The compound showed about 44.23% anti-implantation and 62% of abortifacient effect at their corresponding dose levels tested. The results indicated the antiprogestin activity of 14 β- hydroxy progesterone in albino rats.

Key words : 14β- OHP, Anti-implantation, Abortifacient, Antiprogestin and Contraceptive

INTRODUCTION

Emergency contraceptive pills (ECPs) are an important option for women who have recently had unprotected intercourse and who do not want to become pregnant. Hormonal and non hormonal drugs are being used as ECPs which prevent ovulation or fertilization and possibly post fertilization (implantation of blastocyst).

The Combined Oral Contraceptive Pill (COCP), often referred to as the birth-control pill, or simply "the Pill", is a combination of an estrogen and a progestin, taken orally to inhibit normal female fertility (FDA, 1997). Progestin Only Pills (POP) are the contraceptive pills (mini pills) which contain synthetic progestins only and do not contain estrogen. However currently used estrogen-progestin combination oral contraceptives are undergoing continuing epidemiologic study because of their possible role in increasing the risk of early-onset breast cancer (Chlebowski *et al.*, 2003). Other possible side effects for which questions persist include alteration in lipid profiles and, for older women who smoke, cardiovascular effects as well as possible thromboembolic events.

Synthetic antiprogestins such as mifepristone (RU 486), Onapristone (ZK 98.299) and Liloprestone (ZK 98.734), intercept progesterone action (antagonists) at the molecular level of receptor binding and have the potential to terminate early pregnancy (Puri and Van Look, 1991).Mifepristone (RU-486) is widely used to terminate the pregnancy in earlier stage (Rang *et al.,* 1997). It is a synthetic antiprogestin used as an abortifacient at large single dose (about 300mg) in the first two months of pregnancy and in smaller single dose (10 mg) as an emergency contraceptive (Piaggio *et al.*, 2003). Mifepristone can be used as a regular contraceptive at 2 mg daily to prevent ovulation (Chabbert-Buffet*et al.*,