

Product Data Sheet

Product Name: Fadrozole

Cat. No.: GC19151

Chemical Properties

Cas. No. 102676-47-1

SMILES N#CC1=CC=C(C2CCCC3=CN=CN23)C=C1

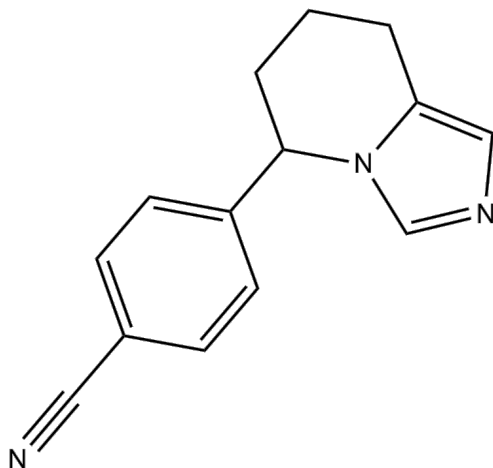
Formula $C_{14}H_{13}N_3$ M.Wt 223.27

Solubility DMSO : ≥ 100 mg/mL (447.89 mM) Storage Store at -20°C

General tips For obtaining a higher solubility , please warm the tube at 37°C and shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

Structure



Protocol

Cell experiment [1]:

Cell lines Prolactin-positive cells

Caution: Product has not been fully validated for medical applications. For research use only.

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Preparation Method Male Wistar rats (175–200g) were killed to extract prolactin-positive cells. Prolactin-positive cells were seeded on 60 culture chamber slides at a final concentration of 2.5×10^5 /ml cells and incubated with Dulbecco's modified Eagle's medium (DMEM) for 7 days. On day 4, medium was changed by fresh DMEM. On day 7, cell cultures were treated with 1 μ M testosterone, 1 μ M Fadrozole and incubated for 1, 3, 6 or 12 hours (5 chambers per treatment). After treatment, the chambers were washed with Dubelcco's sterile PBS, and cells were fixed in Somogy's solution for 1 hour, followed by rinsing in PBS.

Reaction Conditions 1 μ M testosterone, 1 μ M Fadrozole; 1, 3, 6 or 12 hours

Applications Fadrozole alone did not affect prolactin-positive cells. Combination of Fadrozole and testosterone significantly decreases prolactin-positive cells sizes and proliferation rates.

Animal experiment [2]:

Animal models Sprague–Dawley female rats

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Preparation Method	Female rats (180-300g) were mated when 60-120 days old. On day 14 of pregnancy rats were divided into three groups. Group 1 (Fad) rats were implanted s.c. with mini-osmotic pumps containing Fadrozole (300µg/day). Group 2 (control) rats were implanted s.c. with mini-osmotic pumps containing saline. Group 3 (Fad+E₂) rats were implanted s.c. with mini-osmotic pumps containing Fadrozole (300µg/day) and estradiol-17 (E₂) (0.2µg/day, E₂ was dissolved in 0.2ml sesame oil). On day 17 of pregnancy, blood samples were collected from the abdominal aorta of rats in all 3 groups. On day 20 of pregnancy, all 3 groups rats underwent laparotomy under ether anesthesia.
Dosage form	Fadrozole: 300µg/day for 6 days; estradiol-17: 0.2µg/day for 6 days
Applications	Fadrozole treatment significantly reduced E₂ concentration, and led to a fourfold increased intrauterine pressure with smaller uterine tissue framework in pregnant rats. Fadrozole caused fetal abnormalities in pregnant rats, but their weight did not differ from normal fetuses. The combination treatment of Fadrozole and E₂ had similar effect as control groups, indicating that exogenously supplied E₂ could compensate for the loss of endogenous E₂.

References:

- [1] Patil CN, Li W, Wang X. Local transformations of androgens into estradiol by aromatase P450 are involved in the regulation of prolactin and the proliferation of pituitary prolactin-positive cells. J Endocrinol. 2014;222(2):201–12. doi:10.1530/JOE-13-0579.
- [2] Tamada H, Shimizu Y, Inaba T, Kawate N, Sawada T. The effects of the aromatase inhibitor fadrozole hydrochloride on fetuses and uteri in late pregnant rats. Journal of endocrinology. 2004 Feb 1;180(2):337-46.

Background

Fadrozole (CGS 16949A) is a selective, non-steroidal aromatase inhibitor with an IC₅₀ value of

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4.5µM^[1]. Fadrozole has been investigated as a treatment of hormone-responsive breast cancer (estrogen sensitive)^[1]. Aromatase is an enzyme that plays a vital role in converting androgens (like testosterone) into estrogens (like estradiol). Fadrozole can be used to block aromatase and reduces the level of estrogens^[2].

In vitro, prolactin-positive cells were extracted from male Wistar rats. By treating prolactin-positive cells with 1µM Fadrozole alone for 1, 3, 6 or 12 hours respectively, no statistically significant variations in the cellular area and proliferation rates were observed due to absent testosterone and minimal synthesized estradiol^[3]. When treating cells with 1µM Fadrozole and 1µM testosterone, significantly decreased of the size of prolactin-positive cells as well as reduced percentage of proliferation rates were obtained from 3 to 12 hours treatment^[3].

In vivo, Fadrozole (300µg/day) was implanted with mini-osmotic pumps on day 14 of pregnancy Sprague–Dawley rats to reduce the level of estradiol-17 (E₂)^[4]. Fadrozole (1200µg; 4 days) resulted in a significant reduced E₂ concentration and high level of androstenedione and testosterone in pregnant rats^[4]. Fadrozole (1800µg; 6 days) led to a fourfold increased intrauterine pressure with significant smaller uterine tissue framework in pregnant rats^[2,4]. Fadrozole caused fetal abnormalities in pregnant rats, where 20% of fetuses had head injuries while their weight did not differ from normal fetuses^[4].

References:

- [1] Browne LJ, Gude C, Rodriguez H, Steele RE, Bhatnager A. Fadrozole hydrochloride: a potent, selective, nonsteroidal inhibitor of aromatase for the treatment of estrogen-dependent disease. *Journal of medicinal chemistry*. 1991 Feb;34(2):725-36.
- [2] Tiboni GM, Ponzano A. Fetal safety profile of aromatase inhibitors: Animal data. *Reproductive Toxicology*. 2016 Dec 1;66:84-92.
- [3] Patil CN, Li W, Wang X. Local transformations of androgens into estradiol by aromatase P450 are involved in the regulation of prolactin and the proliferation of pituitary prolactin-positive cells. *J Endocrinol*. 2014;222(2):201–12. doi:10.1530/JOE-13-0579.
- [4] Tamada H, Shimizu Y, Inaba T, Kawate N, Sawada T. The effects of the aromatase inhibitor fadrozole hydrochloride on fetuses and uteri in late pregnant rats. *Journal of endocrinology*. 2004 Feb 1;180(2):337-46.

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