

hydrochloride up-regulates expression of the cholesterol transporter gene ABCA1 and the E3 ubiquitin ligase IDOL and reduces LDLR levels^[2]. LXR ligands inhibits platelet aggregation and calcium mobilization stimulated by collagen or CRP. GW3965 hydrochloride (1 or 5 μ M) displays a minor inhibitory effect on fibrinogen binding and P-selectin exposure, when platelets are stimulated with 1 μ g/mL CRP. But using higher concentrations of GW3965 hydrochloride (10 μ M) or T0901317 (40 μ M), the levels of fibrinogen and P-selectin on the platelet surface are reduced^[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

GW3965 hydrochloride induces an increase of neuroactive steroids in the spinal cord, the cerebellum and the cerebral cortex of STZ-rats, but not in the CNS of non-pathological animals. GW3965 hydrochloride treatment induces an increase of dihydroprogesterone in the spinal cord of diabetic animals in association with an increase of myelin basic protein expression^[1]. GW3965 hydrochloride (40 mg/kg, p.o.) strongly induces ABCA1 expression and reduces LDLR expression, and this is accompanied by 59% inhibition of tumor growth, and a 25-fold increase in GBM cell apoptosis in vivo^[2]. GW3965 hydrochloride (2 mg/kg, i.v.) increases bleeding time and modulated platelet thrombus formation in vivo^[3].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay ^[2]

Cells are seeded in 96 wells and are treated after 24 hours with different drugs indicated in each experiment in medium containing 1% FBS or lipoprotein deficient serum. Relative proliferation is determined using Cell Proliferation Assay Kit. Cells are incubated 1.5 hrs after adding tetrazolium salt WST-1 [2-(4-iodophenyl)-3-(4-nitrophenyl)-5-(2,4-disulfo-phenyl)-2H-tetrazolium, monosodium salt] at 5% CO₂, 37°C and the absorbance of the treated and untreated cells are measured using a microplate reader at 420 to 480 nm. Cells seeded in 12 well plates are counted using a hemocytometer, and dead cells are assessed using trypan blue exclusion assays.
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Animal Administration ^[1]

Diabetes is induced in two-month-old male rats by a single i.p. injection of freshly prepared STZ (65 mg/kg) in 0.09 M citrate buffer, pH 4.8. Control animals are injected with 0.09 mol/L citrate buffer at pH 4.8. Hyperglycemia is confirmed 48 h after streptozotocin injection by measuring tail vein blood glucose levels using a glucometer OneTouch Ultra2. Only animals with mean plasma glucose levels over 300 mg/mL are classified as diabetic. Glycemia is also assessed before treatment with Ro5-4864 or GW3965 hydrochloride and before death. Two months after STZ injection, diabetic animals are treated once a week with Ro5-4864 (3 mg/kg) or GW3965 hydrochloride (50 mg/kg). Thus, they receive four subcutaneous injections in a month. Control diabetic rats receive 200 μ L of vehicle (sesame oil). Four-month-old non-diabetic male rats are injected, following the same experimental schedule, with Ro5-4864, GW3965 hydrochloride or vehicle. Rats are killed 24 h after the last treatment.
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Sci Adv. 15 Jul 2022.
- Theranostics. 2020 Jul 11;10(19):8834-8850.
- Cell Death Differ. 2020 Aug;27(8):2433-2450.
- Cancer Lett. 2023 May 5;216208.
- J Ethnopharmacol. 2023 May 24;315:116684.

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- [2]. Guo, Deliang., et al. An LXR Agonist Promotes Glioblastoma Cell Death through Inhibition of an EGFR/AKT/SREBP-1/LDLR-Dependent Pathway. *Cancer Discovery* (2011), 1(5), 442-456.
- [3]. Spyridon, Michael., et al. LXR as a novel antithrombotic target. *Blood* (2011), 117(21), 5751-5761.
- [4]. Collins JL, et al. Identification of a nonsteroidal liver X receptor agonist through parallel array synthesis of tertiary amines. *J Med Chem.* 2002 May 9;45(10):1963-6.
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