

Product Data Sheet

Product Name: Vericiguat (BAY1021189)

Cat. No.: GC32472

Chemical Properties

Cas. No. 1350653-20-1

SMILES O=C(OC)NC1=C(N)N=C(C2=NN(CC3=CC=CC=C3F)C4=NC=C(F)C=C42)N=C1N

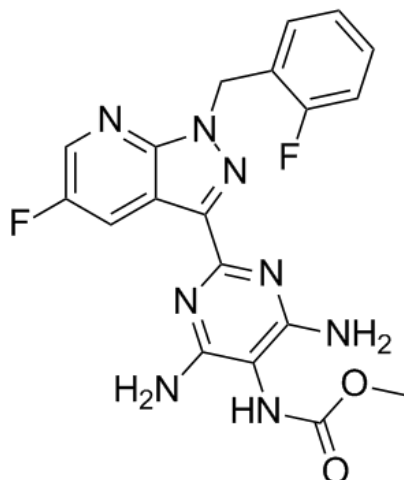
Formula $C_{19}H_{16}F_2N_8O_2$ M.Wt 426.38

Solubility DMSO : 60 mg/mL (140.72 mM); Water : < 0.1 mg/mL (insoluble) 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 Human smooth muscle cells

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Preparation Method

Human smooth muscle cells (HVSMCs) were placed in 6-well plates. When the cell confluence reaches 60% to 70%, replace the medium with serum-free medium. Culture was carried out using SmGM-2 smooth muscle cell growth medium. All experiments were conducted using 3-6 generations of cell cultures. After 24 hours, the cells were treated under the following three different conditions: normal glucose (5.5 mM D-glucose and 24.5mM L-glucose), high glucose (30mM d-glucose), or high glucose+1 μ M vericiguat for 24 hours. The selection of high glucose concentration is based on the previous HVSMCs study, which indicated that 24-hour HG exposure does indeed induce vascular dysfunction, thereby providing a relevant model for evaluating therapeutic intervention measures. To serve as a osmotic pressure control, 24.5mM L-glucose was added to 5.5mM D-glucose in the normal glucose group. All groups were treated with sildenafil (1 μ M) and NO donor DETA NONOate (0.1 μ M). NO donors were given because the HVSCMs system lacked endothelial cells, and thus there was NO endogenous NO production. Sildenafil was added to increase the half-life of cGMP and facilitate the determination of originally unstable compounds. After incubation for 24 hours, the cells were isolated and lysed, and then used to measure cGMP and PKG activities.

Reaction Conditions

1 μ M; 24h

Applications

Vericiguat can rescue cGMP production and sGC activity in a hyperglycemic environment within HVSMCs.

Animal experiment [2]:

Animal models

Male C57/BL6 mice

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Preparation Method	Male C57/BL6 mice (8-10 weeks old) all adapted in a controlled environment with regulated light/dark cycles (12 hours of light /12 hours of darkness), temperature and humidity. The mice were fed standard rodent feed and could freely drink water with a water quality of 1.0% sodium chloride. In order to simulate the real clinical situation, the ligation method of the left anterior descending artery (LAD) was adopted to establish the myocardial infarction (MI) model in mice. The mice were divided into four treatment groups: Sham, Sham+Vericiguat, MI and MI+Vericiguat. Before the operation, mice were anesthetized by intraperitoneal injection of pentobarbital sodium (50mg/kg). Tracheal intubation was performed on mice and respiratory support was provided. The MI group (n=20) and the MI+Vericiguat group (n=20) underwent left thoracotomy and ligation of the LAD with 7-0 silk thread. The success of vascular occlusion was verified by the immediate whitening of the LAD perfusion area and the changes in dynamic electrocardiogram. Suture the chest cavity and skin with 5-0 silk thread. Similar surgeries were performed in the Sham group (n=20) and the Sham+ Vericiguat group (n=20), but LAD was not ligated. Vericiguat treatment (p.o.) was initiated 12 hours after MI and lasted for 28 days at a dose of 10mg/kg/ day. Penicillin (200,000 IU) was injected intramuscularly every day within one week after the operation. All surgeries and subsequent analyses were performed blinding.
Dosage form	10mg/kg/day for 28 days; p.o.
Applications	Vericiguat treatment alleviated cardiac dysfunction and infarction area after myocardial infarction in mice.

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- [1] Polhemus D, Almodiel D, Harb T, et al. Vericiguat prevents high glucose-mediated impaired vascular smooth muscle cGMP production and vasorelaxation[J]. Scientific Reports, 2025, 15(1): 4939.
- [2] Chen T, Kong B, Shuai W, et al. Vericiguat alleviates ventricular remodeling and arrhythmias in mouse models of myocardial infarction via CaMKII signaling[J]. Life Sciences, 2023, 334: 122184.

Background

Vericiguat (BAY1021189) is an oral soluble guanylate cyclase (sGC) stimulant and an inhibitor of breast cancer resistance protein ($IC_{50} = 20\mu M$) as well as OATP1B1 and 1B3 (approximate IC_{50} of 16 and $30\mu M$, respectively)^[1]. Vericiguat inhibited phenylephrine-induced contractions of rabbit saphenous artery rings, rabbit aortic rings, and canine femoral vein rings in a concentration-dependent manner, with IC_{50} values of 798, 692, and $3072nM$, respectively^[2]. Vericiguat can relax the isolated cryptoarterial rings of rabbits that are tolerant to nitrate, with an IC_{50} value of $5.8nM$ ^[3]. Vericiguat has been widely used in the research of cardiovascular diastolic and systolic studies^[4].

In vitro, Vericiguat treatment at a concentration of $1\mu M$ for 24 hours can prevent impaired cGMP production and vasodilation mediated by high glucose in human smooth muscle cells^[5]. Pretreatment with Vericiguat at a concentration of $350\mu g/L$ for 5 minutes directly inhibited platelet activation and aggregation in human isolated platelets, suppressed ATP release induced by thrombin or collagen, and weakened p-selectin exposure stimulated by thrombin^[6]. After 3 hours of treatment, Vericiguat can promote the differentiation of osteoclasts (OC) at a concentration of $500nM$, and inhibit the differentiation of OC at a concentration of $8\mu M$ ^[7].

In vivo, Vericiguat treatment ($10mg/kg/day$; p.o.) for 28 days alleviated cardiac dysfunction and infarction area after myocardial infarction (MI) in C57/BL6 mice^[8]. Intragastric administration of $3mg/kg$ Vericiguat for 3 hours enhanced the vascular distribution in the infarcted area of pig model of ischemia/reperfusion, inhibited pro-inflammatory cells, and reduced collagen deposition^[9]. Vericiguat ($3mg/kg/day$) administered orally for 14 days can inhibit myocardial oxidative stress, and significantly improve angiotensin II-induced left ventricular hypertrophy and fibrosis in male C57Bl/6J mice^[10].

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- [1] Boettcher M, Gerisch M, Lobmeyer M, et al. Metabolism and pharmacokinetic drug–drug interaction profile of vericiguat, a soluble guanylate cyclase stimulator: Results from Preclinical and Phase I Healthy Volunteer Studies[J]. Clinical pharmacokinetics, 2020, 59: 1407-1418.
- [2] Markham A, Duggan S. Vericiguat: first approval[J]. Drugs, 2021, 81(6): 721-726.
- [3] Fritsch A, Meyer M, Blaustein R O, et al. Clinical pharmacokinetic and pharmacodynamic profile of vericiguat[J]. Clinical Pharmacokinetics, 2024, 63(6): 751-771.
- [4] Follmann M, Ackerstaff J, Redlich G, et al. Discovery of the soluble guanylate cyclase stimulator vericiguat (BAY 1021189) for the treatment of chronic heart failure[J]. Journal of medicinal chemistry, 2017, 60(12): 5146-5161.
- [5] Polhemus D, Almodiel D, Harb T, et al. Vericiguat prevents high glucose-mediated impaired vascular smooth muscle cGMP production and vasorelaxation[J]. Scientific Reports, 2025, 15(1): 4939.
- [6] Zhou W, Zhou L, Qi Z, et al. The soluble guanylate cyclase (sGC) stimulator vericiguat inhibits platelet activation and thrombosis[J]. European Journal of Pharmacology, 2025: 177670.
- [7] Sun K, Kong F, Lin F, et al. Vericiguat modulates osteoclast differentiation and bone resorption via a balance between VASP and NF-κB pathways[J]. Mediators of Inflammation, 2022, 2022(1): 1625290.
- [8] Chen T, Kong B, Shuai W, et al. Vericiguat alleviates ventricular remodeling and arrhythmias in mouse models of myocardial infarction via CaMKII signaling[J]. Life Sciences, 2023, 334: 122184.
- [9] Zhu W, Ben Y, Shen Y, et al. Vericiguat protects against cardiac damage in a pig model of ischemia/reperfusion[J]. Plos one, 2023, 18(12): e0295566.
- [10] Harada T, Kondo H, Nakamura K, et al. Soluble Guanylate Cyclase Stimulator Vericiguat Attenuates Angiotensin II-Induced Oxidative Stress and Cardiac Remodeling[J]. Circulation Journal, 2025: CJ-24-0659.

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