# Arhalofenate

**Cat. No.:** HY-14831

**CAS No.:** 24136-23-0

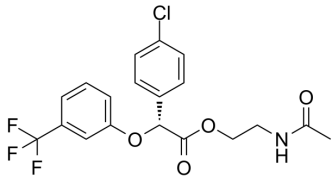
**Molecular Formula:** $C_{19}H_{17}ClF_3NO_4$

**Molecular Weight:** 415.79

**Target:** PPAR

**Pathway:** Cell Cycle/DNA Damage

**Storage:** Please store the product under the recommended conditions in the Certificate of Analysis.



## BIOLOGICAL ACTIVITY

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| **Description** | Arhalofenate (MBX 102) is a selective partial agonist of peroxisome proliferator-activated receptor (PPAR)-γ, used for the treatment of type 2 diabetes. |
| **$IC_{50}$ & Target** | PPAR-γ |
| **In Vitro** | Arhalofenate (MBX 102) is a prodrug ester, that is rapidly and completely modified in vivo by non-specific serum esterases to the mature free acid form Arhalofenate (MBX 102) acid. Arhalofenate (MBX 102) shows a dose-dependent activation of mouse GAL4-PPAR-γ with $EC_{50}$s of appr 12 μM[2].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |
| **In Vivo** | Arhalofenate (MBX 102) (100 mg/kg, p.o.) significantly increases the glucose infusion rate and decreases hepatic glucose output in the clamped state in Zucker Diabetic Fatty (ZDF) rats. Arhalofenate (MBX 102) (60 mg/kg) leads to a dramatic decrease in plasma and also results in a dose-dependent, significant decrease in the insulin resistance indexinsulin levels[1]. Arhalofenate (MBX 102) (100 mg/kg, p.o.) significantly decreases triglyceride, free fatty acid, and cholesterol levels in ZDF rats. MBX-102 significantly reduces fasting blood glucose, confirming that Arhalofenate (MBX 102) is an efficacious antidiabetic agent. Arhalofenate (MBX 102) (100 mg/kg, p.o.) also significantly lowers fasting plasma insulin, and robustly decreases fasting plasma triglycerides after 32 days of treatment in Zucker Fatty (ZF) rats[2].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |

## PROTOCOL

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| **Animal Administration** [1] | Male ZDF rats at 8 wk of age are used in the assay. ZDF rats are single housed and allowed access ad libitum to tap water and chow. ZDF rats are screened into three groups with similar mean plasma glucose levels. ZDF rats are cannulated in the jugular vein and the carotid artery and are allowed to recover at least for 2 d. Rats are dosed with either vehicle or Arhalofenate (MBX 102) (100 mg/kg) by oral gavage for 4-7 d. On the day of the clamp experiment, rats are dosed and food is withdrawn 1 h later. After rats are fasted for 4 h, blood samples are taken from the carotid catheter to measure basal glucose and insulin levels. Experiments are initiated with a priming injection (0.5 mL/rat of 5 μCi/mL of d-[3-$^3$H] glucose) and initiation of a constant infusion of d-[3-$^3$H] glucose tracer (8 μCi/mL) at a rate of 10 μL/min for 60 min. After the 1-h tracer-equilibration period, a post-tracer blood sample is collected for glucose, insulin and d-[3-$^3$H] glucose specific activity (SA) measurements. Infusion of tracer glucose is then discontinued, and insulin infusion is initiated (10 μL/min equivalent to 40 mU/kg/min) along with glucose infusion. The glucose infusion rate is adjusted empirically to achieve plasma glucose level at |

150 mg/dL ± 5% within the next 1.5-2 h. To facilitate this process, blood samples are collected at 10-min intervals for immediate plasma glucose measurements using a glucometer until the end of the study. Clamp is defined by three consecutive glucose measurements that are within the above defined range. Samples (300-400 μL) at the three time points (10-min interval) are collected for glucose, insulin, and d-[3-$^{3}$H] glucose SA measurements.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## CUSTOMER VALIDATION

- Drug Dev Res. 2020 Nov;81(7):859-866.

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## REFERENCES

[1]. Gregoire FM, et al. MBX-102/JNJ39659100, a novel peroxisome proliferator-activated receptor-ligand with weak transactivation activity retains antidiabetic properties in the absence of weight gain and edema. Mol Endocrinol. 2009 Jul;23(7):975-88.

[2]. Chandalia A, et al. MBX-102/JNJ39659100, a novel non-TZD selective partial PPAR-γ agonist lowers triglyceride independently of PPAR-α activation. PPAR Res. 2009;2009:706852.



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