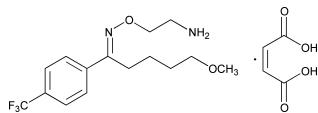


Fluvoxamine Maleate



$C_{15}H_{21}F_3N_2O_2 \cdot C_4H_4O_4$ 434.41

1-Pentanone, 5-methoxy-1-[4-(trifluoromethyl)phenyl]-, *O*-(2-aminoethyl)oxime, (*E*)-, (*Z*)-2-butenedioate (1 : 1).

5-Methoxy-4'-(trifluoromethyl)valerophenone (*E*)-*O*-(2-aminoethyl)oxime, maleate (1 : 1) [61718-82-9].

» Fluvoxamine Maleate contains not less than 98.0 percent and not more than 102.0 percent of $C_{15}H_{21}F_3N_2O_2 \cdot C_4H_4O_4$, calculated on the dried basis.

Packaging and storage—Preserve in well-closed, light-resistant containers. Store at controlled room temperature.

USP Reference standards (11)—*USP Fluvoxamine Maleate RS*.

Identification—

A: *Infrared Absorption* (197K).

B: The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation*, as obtained in the *Assay*.

Melting temperature (741): between 121° and 123°.

Loss on drying (731)—Dry it in vacuum at 80° for 2 hours; it loses not more than 0.5% of its weight.

Residue on ignition (281): not more than 0.1%.

Heavy metals, Method II (231): 0.001%.

Related compounds—

Buffer solution, Mobile phase, Resolution solution, and Chromatographic system—Proceed as directed in the *Assay*.

Identification solution—Dissolve a quantity of maleic acid in *Mobile phase*, and dilute quantitatively, and stepwise if necessary, with *Mobile phase* to obtain a solution having a known concentration of about 0.35 mg per mL.

Standard solution—Use the *Standard preparation*, prepared as directed in the *Assay*.

Test solution—Use the *Assay stock preparation*, prepared as directed in the *Assay*.

Procedure—Separately inject equal volumes (about 20 μ L) of the *Standard solution*, the *Test solution*, and the *Identification solution* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the percentage of impurities in the portion of Fluvoxamine Maleate taken by the formula:

$$5000(C/W)F(r_i / r_s)$$

in which *C* is the concentration, in mg per mL, of USP Fluvoxamine Maleate RS in the *Standard solution*; *W* is the weight, in mg, of Fluvoxamine Maleate used to prepare the *Test solution*; *F* is the response factor of each impurity as given in *Table 1*; *r_i* is the individual peak area of each impurity in the *Test solution*; and *r_s* is the peak area of fluvoxamine maleate in the *Standard solution*. The limits of impurities are specified in *Table 1*. [NOTE—Disregard any peak due to maleic acid or the reagent blank.]

Table 1

Compound Name	Relative Retention Time	Response Factor	Limit (%)
Maleic acid	about 0.19	—	—
5-Methoxy-1-[4-(trifluoromethyl)phenyl]-1-pentanone(<i>E</i>)- <i>O</i> -[2-[(2-succinyl)amino]ethyl]oxime	about 0.50	1.0	0.3
5-Methoxy-4'-(trifluoromethyl)valerophenone(<i>E</i>)- <i>O</i> -(2-aminoethyl)aminoethyl oxime maleate	about 0.67	1.4	0.2
<i>Z</i> -isomer	about 0.79	1.0	0.5
Fluvoxamine	1.0	—	—
4'-(Trifluoromethyl)valerophenone(<i>E</i>)- <i>O</i> -2-(2-aminoethyl)aminoethyl oxime maleate	about 1.18	1.0	0.2
(<i>E</i>)- <i>O</i> -2-(2-Aminoethyl)-4-(trifluoromethyl)- α -phenyl-acetophenone oxime maleate	about 1.74	1.0	0.2
4'-(Trifluoromethyl)valerophenone(<i>E</i>)- <i>O</i> -(2-aminoethyl) oxime maleate	about 2.00	1.0	0.2
5-Methoxy-4'-(trifluoromethyl)valerophenone oxime	about 3.45	0.6	0.2
5-Methoxy-4'-(trifluoromethyl)valerophenone ketone	about 4.2	0.3	0.2
Unknown impurities	—	1.0	0.1
Total	—	—	1.5

Organic volatile impurities, Method I (467): meets the requirements.

(Official until July 1, 2008)

Assay—

Buffer solution—Dissolve about 5 g of 1-pentanesulfonic acid sodium salt and 0.7 g of monobasic potassium phosphate in 620 mL of water. Adjust with phosphoric acid to a pH of 3.00 \pm 0.05.

Mobile phase—Prepare a filtered and degassed mixture of *Buffer solution* and acetonitrile (62 : 38). Make adjustments if necessary (see *System Suitability* under *Chromatography* (621)).

Resolution solution—Transfer about 6 mg of Fluvoxamine Maleate to a 50-mL volumetric flask. Heat the sample at 120° for 10 minutes. Cool down to room temperature, and add 3.0 mL of 0.1 N hydrochloric acid. Heat the solution in a water bath for 10 minutes. Cool down to room temperature, add 50 mg of Fluvoxamine Maleate, and dissolve in 25 mL of *Mobile phase*. Dilute with *Mobile phase* to volume, and mix.

Standard preparation—Dissolve an accurately weighed quantity of USP Fluvoxamine Maleate RS in *Mobile phase*, and dilute quan-

titatively, and stepwise if necessary, with *Mobile phase* to obtain a solution having a known concentration of about 0.05 mg per mL.

Assay stock preparation—Transfer an accurately weighed quantity of about 50 mg of Fluvoxamine Maleate to a 50-mL volumetric flask, dissolve in and dilute with *Mobile phase* to volume, and mix.

Assay preparation—Transfer 5.0 mL of the *Assay stock preparation* to a 100-mL volumetric flask. Dilute with *Mobile phase* to volume, and mix.

Chromatographic system (see *Chromatography* (621))—The liquid chromatograph is equipped with a 234-nm detector and a 4.6-mm \times 25-cm column that contains packing L7. The flow rate is about 1.7 mL per minute. The column temperature is maintained at 40°. Chromatograph the *Resolution solution*, and record the peak responses as directed for *Procedure*: the resolution, *R*, between the *Z*-isomer and fluvoxamine maleate is not less than 3.0 and not less than 5.0 between 5-methoxy-1-[4-(trifluoromethyl)phenyl]-1-pentanone(*E*)-*O*-[2-[(2-succinyl)amino]ethyl]oxime and the *Z*-isomer. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure*: the column efficiency is not less than 5000 theoretical plates; the tailing factor is not more than 2.0;

and the relative standard deviation for replicate injections is not more than 2.0%. [NOTE—For the purpose of peak identification, the approximate relative retention times are given in *Table 1*.]

Procedure—Separately inject equal volumes (about 20 μ L) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the fluvoxamine maleate peaks. Calculate the quantity, in mg, of $C_{15}H_{21}F_3N_2O_2 \cdot C_4H_4O_4$ in the portion of Fluvoxamine Maleate taken by the formula:

$$1000C(r_U / r_S)$$

in which *C* is the concentration, in mg per mL, of USP Fluvoxamine Maleate RS in the *Standard preparation*; and *r_U* and *r_S* are

the peak areas obtained from the *Assay preparation* and the *Standard preparation*, respectively.