

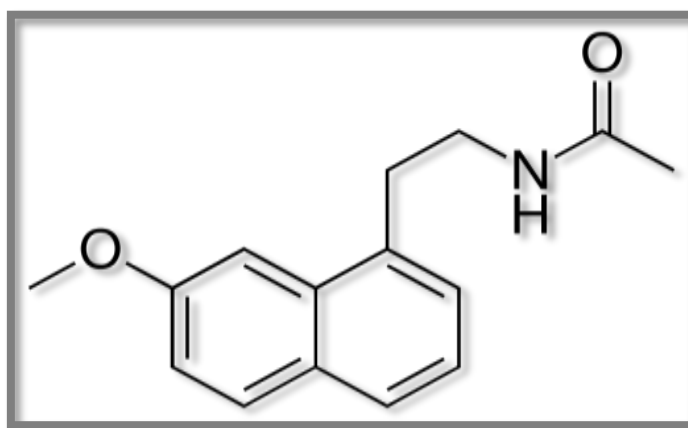
Analytical Profile of Agomelatine

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Molecular Formula¹:C₁₅H₁₇NO₂.

Molecular Weight¹:243.301 g/mol.

Chemical Name¹:N-[2-(7-methoxynaphthalen-1-yl) ethyl] acetamide

Description¹:White or white alike crystal solid powder.

Melting Point¹:108°C.

Category¹:Antidepressant.

Solubility^{1, 2}:Soluble in organic solvents such as ethanol, DMSO, and dimethyl formamide, practically insoluble in purified water.

Adverse Effects^{1, 2}:hyperhidrosis, abdominal pain, nausea, vomiting, diarrhoea, constipation, back pain, fatigue, headache, dizziness, somnolence, insomnia, migraine, anxiety.

Few analytical methods for the estimation of agomelatine have been reported.

Sridhar Thota et al. developed and validated a stability-indicating RP-HPLC method for the determination of agomelatine in human plasma using enable C18 column (150×4.6mm, 5µm) in isocratic mode. The mobile phase consisted of acetonitrile: methanol: water (55:25:20, v/v/v) with a flow rate of 1.0 mL/min (UV detection- 230nm). The Retention time was found to be 4.2 min. Agomelatine was subjected to

stress conditions including acidic, alkaline, oxidation, photolysis and thermal degradation. Agomelatine is more sensitive to acidic and oxidative degradation. The method was validated according to ICH guidelines.³

Vineela P. et al. developed and validated a stability indicating RP-HPLC method for the determination of agomelatine in human plasma using enable thermohypersil C18 column (250×4.6mm, 5µm) in isocratic mode. The mobile phase consisted of phosphate buffer: methanol (60:40, v/v) with a flow rate of 1.0 mL/min (PDA detection- 232nm). The Retention time was found to be 3.3 min. Agomelatine was subjected to stress conditions including acidic, alkaline, oxidation, photolysis and thermal degradation. Agomelatine is more sensitive to heat and oxidative degradation. The method was validated according to ICH guidelines.⁴

Joshi Hitendra S. et al. had developed and validated a simple, precise and stability-indicating high performance thin chromatographic method for analysis of Agomelatine in human plasma. Aluminum foil TLC plates pre-coated with silica gel 60F were used as stationary phase. Dichloro methane and methanol in the ratio of (95:5v/v) were used as mobile phase. A compact band (R_f 0.52±0.002) was obtained for

Agomelatine. Densitometric analysis was performed in absorbance mode at 230 nm.⁵

M. Vijaya Lakshmi et al. developed and validated a simple, efficient, economical RP-HPLC method for the estimation of Agomelatine in human plasma. A Phenomenax C18 column (250 x 4.6mm; 5 μ m) with mobile phase containing water: methanol (20:80% v/v) at a flow rate of 1mL/min was used and quantification was carried at 230nm. The retention time of agomelatine was 5.09 min. The proposed HPLC method was validated as per ICH guidelines and successfully applied for the estimation of agomelatine in bulk and dosage forms.⁶

K. Y. Janga et al. explored a new validated Reverse phase High performance liquid chromatographic method for Agomelatine and estimated entrapment efficiency and drug content in proliposome powder formulation. Central composite design (CCD) with surface response curves employed to obtain suitable liquid chromatographic medium. The most selective mobile phase composition was deduced from the responses of CCD. Agomelatine loaded proliposomal powder with equimolar fractions of hydrogenated soya phosphatidyl choline and cholesterol was acquired by Film deposition technique. Quantification of percentage drug content and entrapment efficiency within formulation was executed in optimized conditions at 230 nm in UV detector allied with Shimadzu HPLC system (Japan). Results Responses accrued from CCD evinced optimized mobile phase composition of acetonitrile : water (55: 45) (v/v) at 250C for complete elution of drug in Phenomenex stainless steel C18 column (250 x 4.6mm,5 μ m) at a flow rate of 1mL/min with retention time of 5.81 \pm 0.26 minutes. A simple, linear, reliable, specific, robust, accurate and precise validated method developed with the aid of Central Composite Design confides it as a potential tool to explicate the quantification of agomelatine in proliposome powder formulation.⁷

Shaheny R. developed and validated a simple and highly sensitive stability-indicating HPLC method for the determination of the new antidepressant agent, agomelatine (AGM) in human plasma. Separation of AGM from its stress-induced degradation products was achieved on a BDS Hypersil phenyl column (250 mm x 4.6 mm i.d., 5 μ m particle size) using methanol-0.05 M phosphate buffer of pH 2.5 (35: 65, v/v) as a mobile phase with fluorescence detection at 230/370 nm. Naproxen was used as an internal standard. The

method satisfied all the validation requirements. The stability of AGM was investigated under different ICH recommended stress conditions including acidic, alkaline, neutral, oxidative and photolytic.⁸

Satish R et al. developed and validated an analytical method based on liquid liquid extraction has been for analysis of agomelatine in human plasma. Fluoxetine was used as an internal standard for agomelatine. A Betasil C18 (4.0100mm, 5mm) column provided chromatographic separation of analytes followed by detection with mass spectrometry. The method involves simple isocratic chromatographic conditions and mass spectrometric detection in the positive ionization mode using an API4000 system. The proposed method has been validated. This validated method was used successfully for analysis of plasma samples from a pharmacokinetic study.⁹

NR Akmar et al. developed and validated stability-indicating RPHPLC method for the determination of Agomelatine in human plasma. RP-HPLC method was developed using Thermo BDS Hypersil C18 column (250 x 4.6 mm, 5 μ m) in isocratic mode. The mobile phase consisted of Acetonitrile: 15mM Phosphate buffer pH 5 (40:60 v/v) with a flow rate of 1.0 mL/min (UV detection-230nm). The Retention time was found to be 6.9 min. Agomelatine was subjected to stress conditions including acidic, alkaline, neutral, oxidation and thermal degradation. Agomelatine is more sensitive to acidic, basic and oxidative degradation. These methods were validated according to ICH guidelines.¹⁰

Liu Y. et al. developed new RP-HPLC method with determination of seven impurities in agomelatine drug substance. Structures of potential impurities were confirmed by NMR and IR analysis. Efficient chromatographic separation was achieved on Hypersil BDS C18 column (250 mm x 4.6 mm, 5 μ m) in gradient mode by using a binary mixture of potassium dihydrogen phosphate (15 mM, pH adjusted to 3.0) and acetonitrile at a flow rate of 1.0 mL/min. A photodiode array detector set at 230 nm was used for detection. Forced degradation studies showed that the proposed method was specific, and agomelatine was found to be susceptible to acidic and alkaline conditions.¹¹

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