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Review:Analytical Method For Determination of Mefenamic Acid in Pharmaceutical and Biological Sample

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Abstract: Mefenamic acid is a nonsteroidal anti-inflammatory drug (NSAID) that has analgesic, anti-inflammatory and antipyretic action. It is used to relieve mild to moderate pains. Mefenamic acid exerts peripheral as well as central analgesic action. the analytical method for identification and quantitative determination of mefenamic acid in pharmaceutical and biological samples.The most commonly methods for the determination of mefenamic acid are chromatographic (HPLC), spectrophotometric, colorimetric,dissolution,various chromatographic methods(HPTLC).A simple method HPLC was developed and validated for mefenamic acid. this method is precise, accurate to analysis mefenamic acid in Pharmaceutical & Biological Sample.[1]

Keywords: mefenamic acid,spectrophotometry,Dissolution,chromatography

INTRODUCTION

Mefenamic acid an analgesic, antipyretic and weaker anti-inflammatory drug. Mefenamic acid is a non-steroidal anti-inflammatory drug with analgesic and antipyretic properties.chemically it belongs to the anthranilic acid derivative class. Mefenamic acid inhibits the enzyme cyclo-oxygenase to exert its anti-inflammatory effect and inhibits the synthesis of prostaglandin to produce analgesic action.mefenamic acid both central and peripheral analgesic action and is a non selective Cox inhibiter, which inhibits both the Cox-1 enzyme and Cox-2 enzyme.

It is white to off white, crystaline powder that darkens on prolonged exposure to light.it melts at 227-232^{o} c insoluble in water,sparingly soluble in chloroform and ether, soluble in 0.1 M NaoH. It is prescribed in the treatment of rheumatoid arthritis, osteoarthritis and other joint disorders.[2]

Mefenamic acid (MFA)N-(2,3-xylyl)anthranilic acid

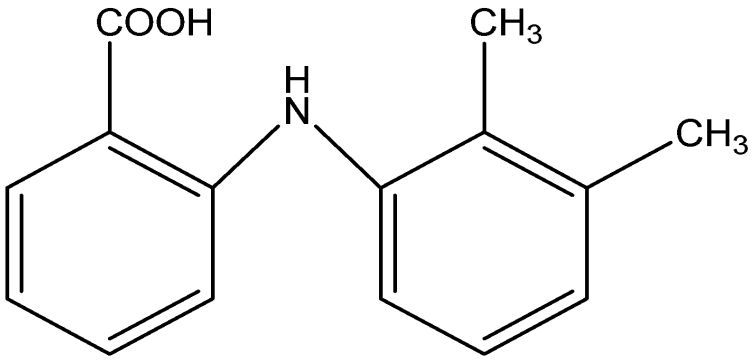

Fig-1:-Chemical Structure of Mefenamic Acid[3]

Adverse effect: Skin rashes,dizziness and other CNS manifestations have occurred.Haemolytic anaemia is a rare.Gastrointestinal Symptoms are the most common adverse effects.Diarrhoea occurs in a large number of patients.

It is contraindicated in gastrointestinal inflammation or ulceration,impairment of renal function.Mefenamic acid prolongs induction of labour by hypertonic saline.[4]

Pharmacokinetics: Oral absorption is slow but almost complete.it is highly bound to plasma protein-displacement interaction can occur;partly metabolizd and excreted in urine as well as bile. Plasma $t^{1/2}$ is 2-4 hours.

Uses: Mefenamic acid as analgesic in muscle, joint and soft tissue pain. It is quite effective in dysmenorrhora and may be useful in some cases of rheumatoid, osteoarthritis.also used in treatment of Headache, dental, postoperative and postpartum pain.

Dose:250-500mg.[5]

Methods for the determination of mefenamic acid:

- Spectrophotometric
- Colorimetric
- Dissolution
- Chromatographic
- Various LC chromatographic method

Sectrophotometric Method:

λmax	Sample	Solvent	Accuracy	Precision	Reference
270nm-0 339.6nm-1 315nm-2	Mefenamic acid+Meloxicam	Methanol+0.1 M NaoH	98.45-0 97.47-1 99.55-2	4.17-0 1.53-1 3.7-2	(6)
285nm	Mefenamic acid	0.1 N NaoH	99.64	0.4839-0.4776	(7)
285nm	Mefenamic acid+Ofloxacin	0.1 N NaoH	99.36	1.423	(8)
233nm-M 245nm-D	Mefenamic acid +Drotaverine Hcl	2.0 M Sodium Benzoate	100.09-M 100.22-D	0.966-M 0.672-D	(9)
588nm	Mefenamic acid	Distilled Water	99.36	1.37	(10)
520nm-Method A 362nm-Method B 602nm-Method C	Mefenamic acid	Acetone	99.25-Method A 100.04-Method B 99.29-Method C	0.56-Method A 1.103-Method 1.575-Method C	(11)
253nm-D 304nm-M	Drotaverine Hcl+Mefenamic acid	Phosphate Buffer PH-6.8	99.06-D 98.70-M	1.154-D 1.129-M	(12)
654nm	Mefenamic acid	0.1 N NaoH	98.7	<1.93	(13)

Colorimetric Method: Colorimetric assay of Mefenamic acid in Pharmaceutical dosage forms using a newly developed chromogenic derivatizing reagent. There agent, diazotized 4-amino-3,5-dinitrobenzoic acid (ADBA), is a dinitrophenylarene diazonium ion, which function via anaromatic ring derivatization technique base on diazo coupling reaction.Diazo coupling of Mefenamic acid with reagent produced Bathochromic Shift.[14]

Dissolution Method: Dissolution testing combined Drotaverine Hcl and Mefenamic acid Tablet formulation(Doverin M) was performed in a Paddle type USP Dissolution Appratus. In these Paddle Type appratus 900ml various buffer and Surfactant media are used at 50 rpm & 37±0.5°c For 45 min. Aliqots of 5.0ml were withdrawn at 5min Interval up to 45 min and Replaced with an equal volume if fresh medium to maintain Sink condition.at the end of the test, The withdrawn Samples were filtered, diluted with Phosphate buffer PH 6.8 & quantified by the developed & validated Sectrophotometric derivative Method (n=3).The amount of dissolved drugs was computed from the respective calibration curves & Then plotted against time. The media in which highest drug release occurred for Doverin-M. This medium was chosen for in vitro Dissloution Studies in Drofem.[15]

Solid Dispersion of Mefenamic acid showed a marked enhancement in Dissolution Rate & Dissolution Efficiency. The order of increasing Dissolution rate was Observed with increase in Crospovidone ratio. The 1:4 ratio Mefenamic acid-CP a 2.26 fold increase in the Dissolution rate of Mefenamic acid was observed with Mefenamic acid-CP(1:4) solid dispersion.The solid dispersion in combined carries gave much higher rates of dissolution than super disintegrants

alone. MACP-PVP solid dispersion gave a 3.47 fold increase in the dissolution rate of Mefenamic acid. Super disintegrants alone or in combination with PVP could be used to enhance the dissolution rate of poorly soluble drug Mefenamic acid.[16]

Chromatographic Method:

Wavelength	Sample	Chromatographic Column	Mobile Phase	Reference
Variable 280nm	Mefenamic acid	Agilent Zorbax Eclipse XDB-C_{18} (150mm x 4.6mm,id 3.5µm	Acetonitrile & 2% Triethylamine (PH adjusted to 4.2 with Phosphoric acid) in a ratio of 60:40	(17)
PDA Detector at 256nm	Ethamsylate, Mefenamic acid	C_{18} (ODS) Sunfire, 250mm x 4.6mm, 5µ(particle size)	Methanol & Water in the ratio of 82:18 v/v	(18)
Uv 256nm	Dicyclomine, Mefenamic acid	Lichrocart c_{18} (250 x 4.60x5im)	50 m M KH_2po_4:Acetonitrile in ratio of 75:25	(19)
215nm	Mefenamic acid, Dicyclomine Hydrochloride	C_8 Luna (150mm x 4.6mm id,5µm)	Acetonitrile:Monobasic potassium dihydrogen phosphate (60:40,v/v)	(20)
275nm	Mefenamic acid	Chromolith(RP-18 e, 100mm x 4.6mm, 5µm)	A:0.1% Formic acid in deionised water, B:100% Acetonitrile	(21)
Uv 220nm	Paracetamol, Acetyl salicylic acid, Mefenamic acid ,Cetirizine dihydrochloride	Nucleodur 100 c_{18} (250 x 4.6mm id,5µm)	Disodium hydrogen phosphate buffer adjused to PH 6.5 using diluted orthophosphoric acid & Acetonitrile (60:40v/v)	(22)
310nm	Tranexamic acid, Mefenamic acid	C_{18} (4.6mm x250mm,5µm)	Buffer & Acetonitrile in the ratio 30:70v/v	(23)
275nm	Paracetamol, Mefenamic acid	Inertsil ODS 3v c_{18} (250 x 4.6mm id,5µm)	Methanol:Buffer(0.02M KH_2PO_4) (75:25), PH 7.1 adjusted with 0.1 N NaoH	(24)
278nm	Mefenamic acid, Diclofenac	Atlantis d c_{18}	0.025 M dibasic potassium phosphate (PH 6.0, adjusted with orthophosphoric acid) & Acetonitrile (65:35v/v)	(25)

Uv 227nm	Captopril, Ibuprofen, Flurbiprofen,Diclofenac sodium,Mefenamic acid	Purospher star c_{18} (5µm, 25x0.46cm)	Methanol:Water (80:20v/v)	(26)
Uv 230nm	Drotaverine Hcl, Mefenamic acid	Thermo BDS Hypersil c_8 (25.0cmx 4.6mm,5µm)	Acetonitrile & Ammonium acetate buffer (20m M, PH 3.5 ±0.05 adjusted with 85% phosphoric acid) in a ratio of 55:45 (v/v)	(27)
254nm	Mefenamic acid	Grace,alltima c_{18} (250 x 4.6mm)	Methanol:Ammonium acetate PH 6 (67:33v/v)	(28)

Various LC Chromatographic Method:

Method	**wavelength**	**Sample**	**Stationary**	**Mobile Phase**	**Reference**
TLC-Densitometry	320nm	Mefenamic acid	Silica gel 60 F 254 plates	Chloroform:Methanol (9.0:0.1v/v)	(29)
HPTLC	254nm	Mefenamic acid, Paracetamol, Dicyclomine Hcl	Aluminium plates precoated with silica gel 60 F254	Toluene:Acetone:Formic acid(10:9.8:0.2)	(30)
HPTLC	287nm	Mefenamic acid, Tranexamic acid	Aluminium plates precoated with silica gel 60 F254	Toluene:Methanol (8:2v/v) & Methanol:Glacial acetic acid (9:1v/v)	(31)
HPTLC	270nm	Mefenamic acid	Merk precoated silica gel 60 F254 (0.2mm thickness) on Aluminium sheets	Chloroform:Methanol: Ammonia in the ratio of 6:4:0.1v/v/v	(32)
HPTLC	254nm	Mefenamic acid	Aluminium 60 F254 plates,(20cm x10cm) with 0.25mm thickness	Toluene:Acetone:Methanol:Ammonia (6.5:2.5:1:0.1v/v/v/v)	(33)

Conclusion: The presented review discusses about various analytical methods for the determination of Mefenamic acid in Pharmaceutical & Biological samples.

New trends & advance for the quantification of Mefenamic acid based on using High Pressure Liquid Chromatography which is generally available.HPLC is the high sensitive,specificity & Faster time. Also HPLC is the automated.HPLC is used for the quantitative &qualitative determination of Mefenamic acid in comparison with the other methods.

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