

ANALYTICAL METHODS FOR THE DETERMINATION OF METHENAMINE HIPPURATE IN PHARMACEUTICAL FORMULATIONS: A COMPREHENSIVE REVIEW

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ABSTRACT

Methenamine Hippurate is widely used as a urinary antiseptic for the treatment and prevention of urinary tract infections. The development of reliable analytical methods is important for the accurate identification and quantification of this drug in pharmaceutical formulations and biological samples. Several analytical techniques, including UV spectrophotometry, High Performance Liquid Chromatography (HPLC), and other chromatographic methods, have been reported for its determination. This review article provides a comprehensive overview of the analytical methods developed for methenamine Hippurate. Particular attention is given to chromatographic and spectroscopic techniques, along with their basic principles, advantages, and limitations. The information presented in this

review may be useful for researchers and analysts involved in pharmaceutical analysis, method development, and quality control of methenamine Hippurate.

KEYWORDS: Methenamine Hippurate, Analytical methods, HPLC, Spectrophotometry, Pharmaceutical analysis.

1. INTRODUCTION

A Urinary Tract Infection (UTI) is an infection that occurs in any part of the urinary system, including the kidneys, ureters, bladder, and urethra. It is one of the most common bacterial infections affecting both men and women, although it occurs more frequently in women due to their shorter urethra. UTIs are mainly caused by microorganisms, particularly bacteria, that enter the urinary tract and multiply, leading to inflammation and infection.

Methenamine Hippurate is a urinary antiseptic used primarily for preventing recurrent urinary tract infections (UTIs). It combines methenamine (also called hexamethylenetetramine) with hippuric acid to create an effective prodrug formulation.

Methenamine Hippurate is the hippuric acid salt of methenamine, with a typical tablet containing 1 g of the compound. The Hippurate moiety enhances solubility and helps maintain an acidic urine pH, while methenamine hydrolyses into formaldehyde in acidic conditions to exert antibacterial effects.^[1]

2. METHENAMINE HIPPURATE^[2]

Methenamine Hippurate is a urinary tract antiseptic (UTIs) and antibacterial drug used for the prophylaxis and treatment of frequently recurring UTIs requiring a long-term therapy.

Class: Urinary antiseptic / Anti-Infective Agent

Mechanism of Action^[3]

In acidic urine (pH below 6), methenamine breaks down to release formaldehyde, which damages bacterial proteins and inhibits growth without promoting resistance. Hippuric acid contributes by acidifying urine and providing mild antibacterial activity, making it effective against common UTIs pathogens like E. coli and enterococci.

Indication^[4]

Methenamine Hippurate is indicated primarily for the prophylaxis (prevention) of recurrent urinary tract infections (rUTIs) in patients without underlying renal tract abnormalities or neuropathic bladder conditions.

ADVANTAGES

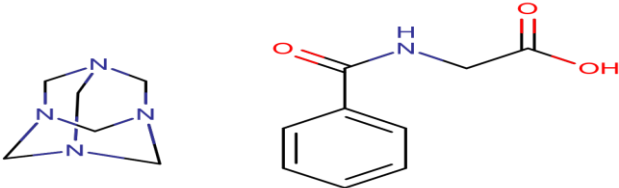
- It works well to prevent recurrent urinary tract infections (rUTIs).
- It starts to work to kill off bacteria in urine after a few hours.
- It has mild side effects.
- It doesn't affect gut flora, so it doesn't get rid of the good bacteria in body needs.

Side effects

Nausea, Upset stomach, Painful urination, Rash

3. DRUG PROFILE^[5]

Table 3.1: Physicochemical Properties of Methenamine Hippurate.

Description	
Chemical structure	
IUPAC Name	2-benzamidoacetic acid, 1,3,5,7 (tetrazatricyclodecane)
Molecular formula	C ₁₂ H ₁₆ N ₄ O ₄
Molecular weight	280.28 g/mol
Category	Urinary antiseptic
CAS Number	5714-73-8
solubility	Freely soluble: water slightly soluble: methanol, ethanol
Mechanism of action	In acidic urine (pH below 6), methenamine breaks down to release formaldehyde, which damages bacterial proteins and inhibits growth without promoting resistance. Hippuric acid contributes by acidifying urine and providing mild antibacterial activity, making it effective against common UTIs pathogens like E. coli and enterococci.
Log P	0.39
pKa value	5.88
Melting point	124-128°C

4. Reported Methods Of Methenamine Hippurate.

4.1: Reported Uv-Spectroscopy Methods Of Methenamine Hippurate.

SR NO.	TITLE	DESCRIPTION	REF NO.
1.	Analytical Method Development and Validation for the Spectrophotometric Estimation of Hippuric Acid Prodrug (Methenamine Hippurate)	Solvent: Distilled water Detection Wavelength: 228 nm Linearity: 2-6 µg/mL	[6]
2.	New validated analytical method for the determination of Methenamine Hippurate (An Antibiotic Agent)	Solvent: buffer Detection Wavelength: 230 nm Linearity: 10-80 µg/mL	[7]

4.2: Reported Hplc Methods Of Methenamine Hippurate.

SR NO.	TITLE	DESCRIPTION	REF NO.
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1.	Method development and validation of Methenamine Hippurate and its related substances in active pharmaceutical ingredients by HPLC	Stationary Phase: X-Bridge C-18 column (250 mm× 4.6 mm) 5µm Mobile Phase: flow rate: 0.6 mL/min wavelength: 210 nm Retention time: 4.674 min Linearity: 50-150 µg/mL	[8]
2.	Determination of methenamine, methenamine mandelate and methenamine Hippurate in pharmaceutical preparations using ion-exchange HPLC	Stationary Phase: Zorbax SCX-300 column Mobile Phase: ACN:0.1 M Sodium Perchlorate Monohydrate (pH 5.8) 70:30 %v/V) flow rate: 1.0 mL/min wavelength: 212 nm Retention time: 2.8 min Linearity: 0.25-50 mM	[9]

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