

## COMPREHENSIVE REVIEW: DEXTROMETHORPHAN (DXM) AND GUAIFENESIN IN COUGH MANAGEMENT

Leelavathi A<sup>1</sup>, Bright Lemuel John N<sup>2</sup>

<sup>1,2,3</sup>Department of PSG College of Pharmacy, Pharmaceutical Analysis, The Tamilnadu Dr. M.G. R Medical university, Chennai. Peelamedu, Coimbatore- 641 004, Tamil Nadu, India.

Corresponding author: A. Leelavathi,

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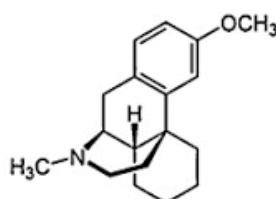
### ABSTRACT

Dextromethorphan (DXM) and Guaifenesin are commonly used medications, often in combination, for the treatment of cough and associated symptoms. Dextromethorphan, a synthetic morphinan derivative, acts as a cough suppressant by inhibiting the cough reflex in the central nervous system. It is widely utilized due to its effectiveness and relatively low potential for abuse compared to opioid-based cough suppressants. Guaifenesin, on the other hand, is an expectorant that works by thinning and loosening mucus in the airways, making it easier to cough up and expel. When used together, these medications offer a comprehensive approach to managing cough and related respiratory issues. This abstract provides an overview of the pharmacological properties, clinical efficacy, safety profiles, and potential adverse effects associated with the use of Dextromethorphan and Guaifenesin, highlighting their role in the treatment of cough and respiratory conditions. Therefore, the main goal of this estimation of Dextromethorphan and Guaifenesin within the pharmaceutical method is in each qualitative and quantitative terms in this assessment article, we have short UV/Vis Spectroscopy, LC MS technique etc. Based totally methods for estimation of Dextromethorphan and Guaifenesin for individual and different drug combination. In end, this review article will help to investigate scholars for similarly approach improvement for drug estimation in pharmaceutical dosage form.

**Keywords-** Dextromethorphan, Guaifenesin, Analytical Method, UV Spectrometry, LC MS Method, Respiratory conditions.

### 1. INTRODUCTION

Dextromethorphan (DXM) is a (1S,9S,10S)-4-methoxy-17-methyl-17 azatetracyclo [7.5.3.01,10.02,7] heptadeca-2(7),3,5-triene hydrobromide widely used over-the-counter medication primarily known for its antitussive (cough-suppressant) properties. Chemically classified as a morphinan derivative, DXM acts centrally on the cough center in the brain, effectively reducing the urge to cough. It is often included in various cough and cold medications, both alone and in combination with other active ingredients, to alleviate cough symptoms associated with conditions such as the common cold or bronchitis. Beyond its cough-suppressant effects, DXM also exhibits activity as an NMDA receptor antagonist at higher doses, leading to dissociative and hallucinogenic effects. This property has led to its recreational use and has raised concerns about abuse potential and addiction. Consequently, in many regions, DXM-containing products are regulated and may require age restrictions or be available only behind the counter. Despite its widespread use, caution is advised when consuming DXM-containing products, particularly at higher doses, due to the risk of adverse effects and potential interactions with other medications. Additionally, misuse or abuse of DXM can lead to serious health consequences, including overdose. Therefore, it is crucial to use DXM medications as directed and to seek medical advice if experiencing any adverse reactions or concerns about its use.



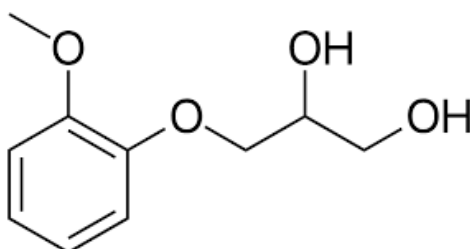
**Fig.1** Structure of Dextromethorphan

Guaifenesin is an expectorant medication commonly used to relieve chest congestion associated with respiratory conditions such as the common cold, bronchitis, and sinusitis. It works by thinning and loosening mucus in the airways, making it easier to cough up and expel from the body. Guaifenesin is available over-the-counter and is often found in various cough and cold medications, either alone or in combination with other active ingredients. As an expectorant, guaifenesin helps to alleviate symptoms such as coughing, chest congestion, and difficulty breathing by

promoting the removal of excess mucus from the respiratory tract. It does not directly suppress coughing but rather facilitates the natural process of clearing mucus from the airways. While guaifenesin is considered safe for most people, individuals with certain medical conditions or taking specific medications should consult their healthcare provider before using guaifenesin-containing products. Additionally, it is essential to stay hydrated while taking guaifenesin to help thin mucus effectively. Overall, guaifenesin serves as a valuable tool in managing respiratory congestion and can provide relief for individuals experiencing symptoms of respiratory infections or other conditions affecting the airways.

**Table 1:** Properties of Dextromethorphan

S.NO	PROPERTIES	DEXTROMETHORPHAN
1.	Brand Name	Koffex DM,
2.	Molecular weight	352.3 g/mol
3.	Boiling point	394.9 °C
4.	Molecular formula	C <sub>18</sub> H <sub>25</sub> NO
5.	Uses	To relieve coughs due to colds or influenza (flu).
6.	PKa	9.85
7.	$\lambda_{\max}$	230 nm



**Fig.2** Structure of Guaifenesin

## ANALYTICAL METHOD AND DEVELOPMENT

Development and validation of analytical methods play a crucial role in pharmaceutical product assembly as well as medication discovery and advancement. It comprises determining a drug substance's toxicity and purity. Development of analytical methods is the process of choosing an exact assay method to ascertain a formulation's composition. It involves demonstrating that an analytical technique can be used in a lab to determine the concentration of future samples. The procedures and acceptance criteria outlined in the ICH guidelines Q2 must be applied when developing analytical techniques in GMP and GLP environments (R1). In the discovery, development, and production of pharmaceuticals, analytical method development and validation are crucial processes. The following literature review reveals that single and combined approach has been described for the combination of Dextromethorphan and Guaifenesin. Various analytical methods like Spectrophotometric, RP- HPLC and HPTLC were reported for estimation of Dextromethorphan and Guaifenesin in bulk form. Spectrophotometric method and LC-MS/MS method were reported for simultaneous estimation of in Dextromethorphan and Guaifenesin combined dosage form.

**Table 2:** Properties of Guaifenesin

S.NO	PROPERTIES	GUAIFENESIN
1.	Brand Name	Mucinex
2.	Molecular weight	198.2158 g/mol
3.	Boiling point	215 °C
4.	Molecular formula	C <sub>10</sub> H <sub>14</sub> O <sub>4</sub>
5.	Uses	To help clear mucus or phlegm

6.	PKa	2.53
7.	$\lambda_{\max}$	272 nm

## SAMPLE PREPARTION

## SOLUBILITY

According to Biopharmaceutics Classification System (BCS), classification of Dextromethorphan and Guaifenesin falls under BCS class-II, meaning it has low solubility and high permeability. The solubility of the drug was tested in solvents routinely used for analytical methodology.

**Table 3: SPECTROPHOTOMETRIC METHODS**

S.NO	METHOD	DESCRIPTION	SOLVENT	$\lambda_{\max}$	REF.NO
1	Development and Validation of UV Spectroscopic Method for Estimation of Guaifenesin in Tablet Dosage Form	<b>Linearity:</b> 6-14 $\mu\text{g/ml}$	Methanol	269 nm	6
2	Sensitive Spectrophotometric Method for Quantitation of Guaifenesin and	<b>Linearity:</b> 5–45 $\mu\text{g mL}^{-1}$	Water	550 nm	7
3	A New and Sensitive UV Spectrophotometric Method for the Determination of	<b>Linearity:</b> 2.5-15 $\mu\text{g/mL}$	Methanol	224nm	8
4	UV Spectrophotometric Method for Estimation of Dextromethorphan in Bulk and Syrup Formulation by Area Under Curve Method	<b>Linearity:</b> 10 to 50 $\mu\text{g/ mL}$	Methanol	295 nm	9
5	Simultaneous UV Spectrophotometric Determination of Cetrizine and Dextromethorphan in Tablet Dosage Form	<b>Linearity:</b> 10-30 $\mu\text{g/mL}$	Methanol	254 nm	10

## CHROMATOGRAPHY

Pharmaceutical samples. Analytical methods for the determination of Dextromethorphan and Guaifenesin pharmaceutical dosages forms using LC-MS/MS are shown in Table 4.

**Table 4: Summary of LCMS methods to determine Dextromethorphan and Guaifenesin in biological samples.**

S.NO	METHOD	MOBILE PHASE	STATIO NARY PHASE	FLO W RATE	RETENTIO N TIME	RETEN TION Factor	$\lambda_{\max}$	REF. NO
1	Simultaneous determination of dextromethorphan, dextrophan, and guaifenesin in human plasma using semi-	Acetonitrile: Water (95:05 v/v)	Shimpak C8 column (5 $\mu\text{m}$ , 15.0 cm x 4.6 mm)	0.7 ml/min	Less than 10 min		210nm	11

	automated liquid/liquid extraction and gradient liquid chromatography tandem mass spectrometry							
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Analytical methods for the determination of Dextromethorphan and Guaifenesin in pharmaceutical dosages forms using HPLC are shown in Table 5.

Table 5: Summary of HPLC methods to determine Dextromethorphan and Guaifenesin in biological samples.

S.NO	METHOD	MOBILE PHASE	STATIONARY PHASE	FLOW RATE	RETENTION TIME	$\lambda_{\max}$	REF.NO
1	High-Pressure Liquid Chromatographic Assay of Dextromethorphan Hydrobromide, Guaifenesin, and Sodium Benzoate in an Expectorant Syrup	Methanol: Water (80:20 v/v)	ODS C18 reversed phase column	1 mL/min		225 nm	12
2	Development and Validation of a Stability-Indicating RP-HPLC Method for the Simultaneous Estimation of Guaifenesin and Dextromethorphan Impurities in Pharmaceutical Formulations	Acetonitrile: Water (60:40 v/v)	Sunfire C18, 250 × 4.6 mm, 5 $\mu$ m	1.10ml/min	3.71min	224 nm	13
3	Method development and method validation of guaifenesin and dextromethorphan by RP-HPLC	0.1M KH <sub>2</sub> PO <sub>4</sub> : Methanol (60:40)	C18, 250X4.6mm, 5 $\mu$ m	1mL/min	3.4 min	250 nm	14
4	Determination of guaifenesin and dextromethorphan in a cough syrup by HPLC with fluorometric detection	acetonitrile and methyl alcohol (v/v, 62:23:15).	C18 column	1 mL/min		277 nm	15

5	Determination Of Guaifenesin And Dextromethorphan In A Cough Syrup By HPLC With Fluorometric Detection	phosphate buffer (0.2 M, pH=2), acetonitrile and methyl alcohol (v/v, 62:23:15).	C18 Column 5 $\mu$ m 4.6 $\times$ 250 mm	1.3 ml/min	3.6 min	277 nm	16
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## 2. CONCLUSION

This article provides insights into the enhanced activity of Dextromethorphan and Guaifenesin in combination with other drugs. The review offers a comprehensive overview of various analytical methods documented in the literature for the determination of Dextromethorphan and Guaifenesin. Different analytical techniques, such as UV spectroscopy and HPLC, are explored for individual as well as combination analysis. Furthermore, the article delves into the pharmacological actions, chemical structures, solubility, and other pertinent characteristics of Dextromethorphan and Guaifenesin. It underscores the scarcity of reported methods for each drug and their combination, highlighting the need for further research in method development. This review serves as a valuable reference for future endeavors in method development and validation, providing evidence of the characteristics of both drugs and their combinations.

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