# HPLC method for determination of dimetindene maleate in pharmaceutical preparations and environmental water samples: Application to content uniformity testing

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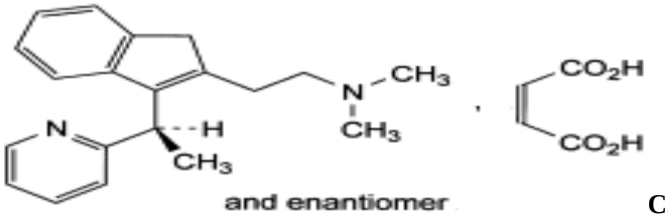
**ABSTRACT - Arapid assay method based on high performance liquid chromatography (HPLC) have been developed for the determination of dimetindene maleate in pharmaceutical formulations and environmental water samples. The HPLC determination was carried out on a reversed phase $C_{18}$ column using acetate buffer pH(4.0): Acetonitrile as mobile phase (65:35), at a flow rate1.0 ml.min$^{-1}$ with UV-detection at 254 nm. A recti lines relationship was observed between 2.0-7.0 µg.ml$^{-1}$dimetindene maleate. The proposed method have been successfully applied to the determination of dimetindene maleate in various dosagepharmaceuticals forms and environmental water samples**

**Keywords:** Dimetindenemaleate, determination,HPLC, pharmaceuticals. environmental water samples

## INTRODUCTION

Dimetindene maleate: N,N-Dimethyl-2-[3-[(RS)-1-(pyridin-2-yl)ethyl]-1H-inden-2-yl]ethanamine (Z)-butenedioate. With a molecular formula of $C_{24}H_{28}N_2O_4$ and molecular weight of (408.8). Its structural formula is as follows [1]




**C24H28N2O4 408.5**

Is antihistamine agent may be considered as a derivative of the un standard propyl amines [1-3] , it is mildly sedative and is reported to have mast-cell stabilizing properties. It is used for the symptomatic relief of allergic conditions including urticarial and angioedema and rhinitis and in pruritic skin disorders. It is also used in compound preparations for the symptomatic treatment of coughs and the common cold [4,5] . The literature revealed that dimetinden maleate has been determined by mean of a few analytical methods. These include HPLC[6] , densitometry [7] , TLC Method[8] , capillary electrophoresis [9] . The spectrophotometric methods using different reagents like potassium permanganate [10] , p-chloranilic acid [11] , and7,7,8,8-tetracyano-quinodimethane (TCNQ) [12] have also been reported for its determination. These methods suffer from some drawbacks like large number of solvent for the extraction, instability of color, use of toxic reagents etc. in the present work, a simple sensitive HPLC methods for the determination of dimetindene maleate in pure form and in pharmaceutical preparations.

## EXPERIMENTAL

### Apparatus

The chromatographic system consisted of an shimadzu HPLC model LC-20AT with UV detector model SPD-20A and C18 supelco column (25cm × 4.6mm), 5 microns. HPLC conditions are given in Table[1]

Table1: HPLC conditions

| | |
|---|---|
| Column | Supelco $C_{18}$(25cm×4.6mm),5 µ.m |
| Detector | 254 nm |
| Mobile phase | Acetate buffer pH(4.0): Acetonitrile as mobile phase (65:35) |
| Retention time | 12.5 min |
| Flow rate | 1.0ml/min |
| Temperature | ambient |
| Injection volume | 10 µl |

### Reagents

All chemicals used were of analytical or pharmaceutical grade and high-purity water was used throughout and dimetindene maleate standard material was provided from AL-hokamaa company for pharmaceutical industries (HPI) Mosul-Iraq.

A 10ppm of dimetindene maleate was prepared by dissolve 0.01gm of dimetindene maleate in 1L distilled water. Acetate buffer PH 4.0, this solution was prepared by dissolving 4.1 gm of sodium acetate and 2.85 ml glacial acetic acid dilute to 50 ml by distilled water. Take 10 ml of this solution and diluted to 1L by distilled water. (Adjust the PH to 4.0 by glacial acetic acid. The mobile phase used consisted of acetate buffer PH 4.0 and acetonitrile (65:35)

### Recommended Procedure

Chromatographic separation was achieved at ambient temperature on a reversed phase $C_{18}$ column (25cm × 4.6mm), 5 microns using a mobile phase consisting of acetate buffer (PH4.0)- acetonitrile (65:35) at flow rate. 1.0ml.min$^{-1}$. the detector wavelength was set at 254 nm.

Calibration graph:working standard solution equivalent to2.0-7.0 µg.ml$^{-1}$dimetindenemaleate were prepared by appropriate dilution of standard solution with water. 10µL a aliquot of each solution was injected on to the column in a duplicate and the chromatograms were recorded. Calibration graph was constructed by plotting the mean peak area versus concentration of dimetidenemaleate. The concentration of the unknown was read from the calibration graph or calculated from the regression equation derived from the concentration and peak area data.

### Procedures for pharmaceutical preparations:

### Oral drops and syrup:

The content of 5 bottles provided from AL-Hokamaa company for pharmaceutical industries (HPI) Mosul-Iraq)were mixed well in 1L dried beaker. Aliquots equivalent to 10 mg of dimetindene maleate were transferred into 1L volumetric flasks anddiluted with distilled water to the volume. The determination of dimetindene maleate proceeded as described under recommended procedure

### Capsules:

The content of 10 capsules were mixed thoroughly, an accurate weight equivalent to 10 mg of dimetindene maleate was transferred into 100ml beaker added 50 ml of water and mixed well for 30 min, filtered, transferred quantitatively to 1L volumetric flask and completed to the volume. The determination of dimetidene maleate proceeded as described under recommended procedure.

### Procedure for water samples:

To demonstrate the practical applicability of the proposed method. The tap and river water samples were collected in polyethylene container cleaned with nitric acid ,and filtered through Whatman No.41 filter paper. Filtered samples were stored at 4 $C^0$ until analyzed which shows negative results found to be free from of dimetidene maleate,synthetic samples were prepared by adding known concentration of dimetidene maleate to each samples prior analysis in the range from 2.0-7.0 ppm The determination ofdimetidene maleate proceeded as described under recommended procedure. Calculate the percentage recovery using a calibration graph previously prepared.

## RESULTS AND DISCUSSION

The development of HPLC methods for the determination of drugs has received conceder-able attention in recent years because of their importance in the quality control of drugs and pharmaceutical products. HPLC-UV is one of the most popular, efficient and cost effective methods of detection for microanalysis and separation of pharmaceuticals in different environmental matrices. The hyphenation of HPLC with UV is useful for a large number of pharmaceuticals as most of these are amenable to UV detection[13-15]. The aim of this study was to develop a rapid HPLC method for the determination of Dimetindene maleate. A solution of dimetindene maleate was injected in duplicate on to the column and was monitored by UV-detection at 254nm. The composition and PH of the mobile phase were varied to optimize the chromatographic conditions. A mobile phase consisting of acetate buffer (PH 4.0): acetonitrile (65:35) was after several preliminary runs. Acetonitrile and acetate buffer increase the solubility of dimetindene and prevent its adherence to the packing material in the column. At a flow rate of 1.0 ml.min$^{-1}$, the retention time for dimetindene maleate was 12.5 min. (Figure. 1).

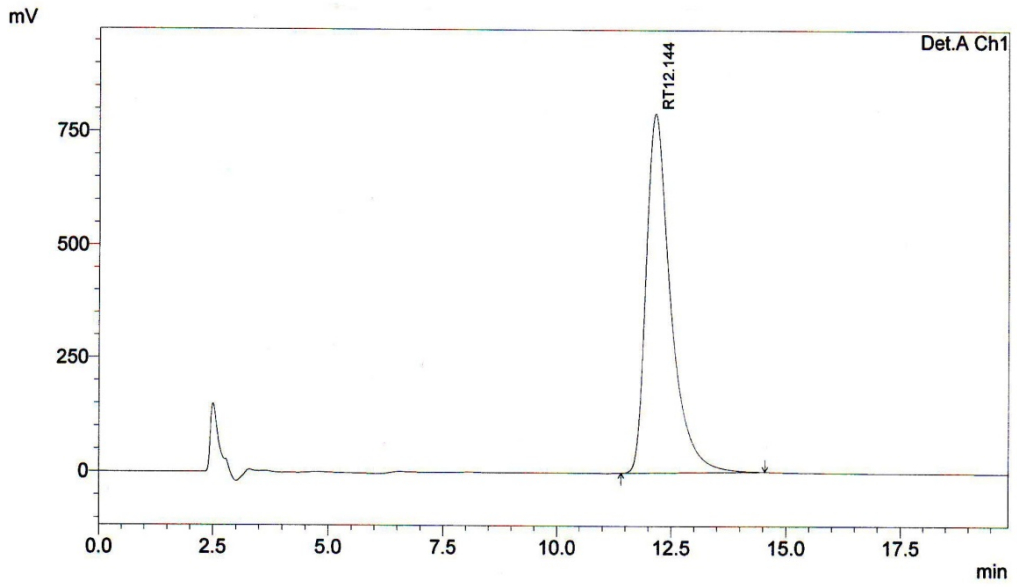



Figure1: Typical chromatogram (dimetindenemaleate 5 µg.ml$^{-1}$).

The calibration curve of dimetindenemaleate was constructed by plotting the peak area against concentration of dimetindenemaleate, it was found to be linear with a correlation of (r = 0.9989) , the representative linear regression equation being Y=151.57 X– 4.5714 were Y is the mean peak area and X is the concentration in µg/ml. (Figure .2).

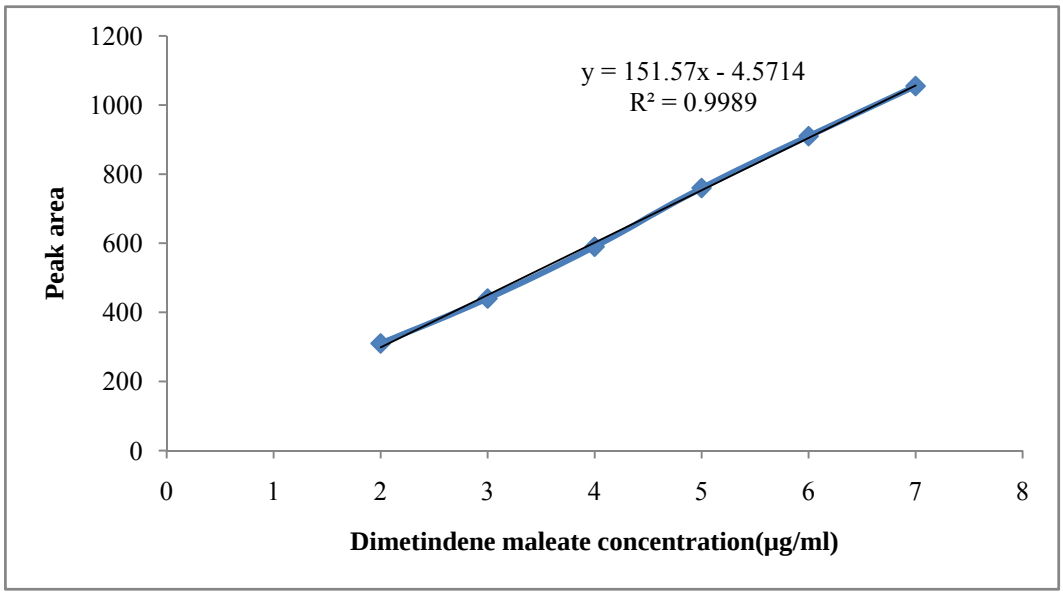



Figure 2:Calibration curve fordimetidene maleate

**Accuracy and precision**

To determine the accuracy and precision of the methods, pure dimetidene maleate solutions containing three different concentrations were analyzed in ten replicated. The results obtained from this investigation are summarized in table (2). The percent relative error which is an index of accuracy is <1.8% and is indicative of good accuracy.The peak-area based and retention time based RSD values were lessthan1.9 %.

Table 2:Accuracy and precision of the method

| Dimetindene taken μg.ml$^{-1}$ | Er (%) | RSD% |
|---|---|---|
| 2 | 0.94 | 1.85 |
| 5 | 1.74 | 0.75 |
| 7 | 1.76 | 1.58 |

**Analytical application**

The proposed methods were successfully applied to the assay of dimetindene maleate in oral drops, syrups and capsules. The results obtained are presented in table (3) and reveals that there is close agreement between the results obtained by the proposed methods and the label claim and the results of water samples Table(4) show that the recovery values obtained were closed to 100%.

Table 3: Determination of dimetindenemaleate formulations

| Pharmaceutical formulations | Label amount | Found* |
|---|---|---|
| Oral drops | 0.1% | 0.103% |
| syrup | 0.01% | 0.01% |
| Capsules | 4mg/caps | 4.03mg/caps |

Table4: Determination of dimetindenemaleate in water samples

| Water samples | Dimetindenemaleate(μg.ml$^{-1}$) taken found | % Recovery(n=10) |
|---|---|---|
| Tap water | 2.01. 994 | 99.7 |
| | 3.0 3.002 | 100.066 |
| | 7.06.9992 | 99.988 |
| River water | 2.0 1. 996 | 99.8 |
| | 3.0 2.995 | 99.83 |
| | 7.0 7.003 | 100.043 |

**Application the method to uniformity of dosage units (content uniformity)**

The proposed method proved to be suitable for the content uniformity test, where a great number of assays on individual capsules are required. Data presented in Table[5] indicate that the proposed method can accurately and precisely quantities dimetindenemaleate(4mg) in its commercially available capsules. The mean percentage (with RSD) of the labeled claim found in ten capsuleswas (1.4%) which falls within the content uniformity limits specified by the USP 33and the JP XVII[16,17].

Table (5):Content uniformity testing of dimetindenemaleatecapsulesusing the proposed method

| Parameter | % of the label claim |
|---|---|
| Capsule NO. 1 | 101. 26 |
| Capsule NO. 2 | 101. 54 |
| Capsule NO. 3 | 98. 87 |
| Capsule NO. 4 | 99.23 |
| Capsule NO. 5 | 101.81 |
| Capsule NO. 6 | 101. 65 |
| Capsule NO. 7 | 98.58 |
| CapsuleNO. 8 | 98. 52 |
| CapsuleNO. 9 | 101.65 |
| CapsuleNO. 10 | 100.46 |
| Mean ( $\bar{x}$ ) | 100.39 |
| % RSD | 1.4 |
| Max. allowed unit [16,17] | ±15% |

## CONCLUSIONS

The method developed is a simple, selective and offers the advantages of high sensitivity and a wide range of determinations without the need for heating or solvent extraction. The proposed method have been successfully applied to the determination of dimetindene maleate in various dosagepharmaceuticals forms and environmental water samples

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