Chapter 3

Gas chromatographic methods for the determination of drugs
Determination of doxepin hydrochloride in bulk and pharmaceutical preparations by gas chromatography

ABSTRACT

A gas chromatographic method has been developed for the determination of doxepin hydrochloride (DH) in pure and pharmaceutical preparations. The detection was carried out using flame ionization detector. Separation was achieved on a 3% OV-101 stainless steel column of 6 feet in length with an internal diameter of 2 mm. Nitrogen was used as a carrier gas at a flow rate of 1.8 kg/cm²/min. The column temperature was maintained at 250 °C while the temperature of injection port and detector were maintained at 280 °C and 300 °C, respectively. Metaprolol succinate (MPS) was used as an internal standard. The procedure gave a linear response over the concentration range of 0.5-15 mg/ml with sufficient reproducibility. The method has been applied successfully for the determination of DH in pure and pharmaceutical formulations. The excipients present in the formulations did not interfere with the assay procedure. The recovery values were found to be in the range of 98.4-100.2% with RSD values less than 1%.

The results of this chapter have been communicated for publication.
**General drug profile**

**Commercial name**: Doxepin hydrochloride  
**Chemical name**: (3E)-3-(6H- benzo[c] [1] benzoepin-11-ylidene)-N,N-dimethylpropan-1-amine hydrochloride  
**Structure**  

\[
\text{\begin{tikzpicture}
\draw[blue,very thick] (0,0) circle (0.5); 
\draw[blue,very thick] (1.5,0) circle (0.5); 
\draw[blue,very thick] (0,1.5) circle (0.5); 
\draw[blue,very thick] (1.5,1.5) circle (0.5); 
\draw[blue,very thick] (0,0) -- (1.5,1.5); 
\draw[blue,very thick] (0,1.5) -- (1.5,0); 
\draw[blue,very thick] (0,1.5) -- (0,0); 
\draw[blue,very thick] (1.5,1.5) -- (1.5,0); 
\draw[blue,very thick] (0,0) -- (0,1.5); 
\draw[blue,very thick] (1.5,0) -- (1.5,1.5); 
\node at (0,-0.5) {CHCH\_2\_CHN(CH\_3)\_2}; 
\node at (1.5,-0.5) {HCl}; 
\end{tikzpicture}}
\]

**Molecular formula**: C\textsubscript{19}H\textsubscript{22}C\textsubscript{1}NO  
**Molecular weight**: 315.83  
**Description**: A white crystalline powder  
**Solubility**: Easily soluble in water  
**Category**: Tricyclic antidepressant

**INTRODUCTION**

DH is a tricyclic antidepressant used in the treatment of mixed depression, anxiety, panic disorders, sleep disorders and other forms of depression. It is also used occasionally to treat chronic pain, peptic ulcer disease and some skin conditions. It is extensively used in the treatment of emotional and psychiatric disorders in which the major symptom is depression, particularly endogeneous depression. The tricyclic antidepressants are the most widely used drugs for the treatment of depression. They display a potent central anticholinergic activity and can alter the activity of both noradrenergic and serotonergic pathways.
The official methods [1,2] recommend the determination of DH by titration in non-aqueous solvents or by UV-spectrophotometry. Due to its characteristic structure, it exhibits a number of interesting analytical properties. The most important of these is the liability to form with the halide and thiocyanate complexes of some metals, e.g., bismuth, antimony, palladium and mercury or with some organic substances of sparingly soluble, colored precipitates which can be quantitatively extracted with some organic solvents and may be determined by spectrophotometric methods [3]. Another existing method for the determination of DH is based on the direct reaction of it with Co(II)-picrate [4] followed by complexometric titration of an excess of metal. In this method, a large number of organic substances, drugs, and excipients interfere significantly. This fact justified the development of different analytical techniques, e.g., polarography [5] and spectrophotometry [6-10]. Gas liquid chromatography [11,12], high performance liquid chromatography [13-22], GCMS [23,24], thin-layer chromatography [25], and capillary electrophoresis [26,27] methods have been employed for the determination of DH in biological fluids. Some studies have proposed potentiometric sensors [28] to be used in the determination of doxepin cation in a substance and in its pharmaceutical preparations.

Gunnar et al. have reported gas chromatographic method [11] for the assay of the drug which involved tedious procedure. The method needs to prepare derivative of the drug for its determination and the detection was carried out with electron capture detection. Another GC method for the assay
of DH was described by Cyr and Lawrence [12]. This method does not discuss the direct assay of DH. It demonstrates the assay of isomers of DH, that too in raw material and capsules.

Literature survey revealed that no attempt has been made for the assay of pure DH in pharmaceutical preparations using MPS as an internal standard. The present work describes the details of determination of DH by GC method.

**EXPERIMENTAL**

**Stock solutions**

**Standard drug solution**

1.5 g of the pure DH was accurately weighed, dissolved in methanol and diluted up to the mark in a 50 ml volumetric flask with the same solvent.

**Internal standard solution**

1.5 g of pure MPS was accurately weighed and dissolved in methanol in a 50 ml calibrated flask.

**Standard working solutions**

Standard working solutions of DH and MPS were prepared in methanol. Aliquots from each working solution were combined and diluted with methanol to give solutions containing 0.5-15 mg/ml of DH and fixed amount of MPS (20 mg). Studies on the stability of analytes in standard working solution showed that there were no decomposition products in the chromatogram during analytical procedure.
Pharmaceutical preparation

Tablets

Ten tablets containing DH were taken and finely powdered. An amount equivalent to 100 mg of the drug was weighed accurately and transferred into a 100 ml beaker. Using a mechanical stirrer, the powder was completely disintegrated in methanol. The solution was filtered and the filtrate was made up to 50 ml with the same solvent.

Capsule

Mixed contents of 10 capsules containing DH were taken. An amount equivalent to 100 mg of the drug was weighed accurately and transferred into a 100 ml beaker. Using a mechanical stirrer, the powder was completely disintegrated in methanol. The solution was filtered and the filtrate was made up to 50 ml with the same solvent.

Operating conditions

<table>
<thead>
<tr>
<th>Column</th>
<th>3% OV-101 (60-80 mesh) packed into a steel column of 6 feet in length and internal diameter of 2 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solvent</td>
<td>Methanol</td>
</tr>
<tr>
<td>Internal Standard</td>
<td>MPS</td>
</tr>
<tr>
<td>Carrier gas</td>
<td>Nitrogen</td>
</tr>
<tr>
<td>Column temperature</td>
<td>250 °C</td>
</tr>
<tr>
<td>Injection port temperature</td>
<td>280 °C</td>
</tr>
<tr>
<td>Detector temperature</td>
<td>300 °C</td>
</tr>
<tr>
<td>Flow rate</td>
<td>2.0 kg/cm²/min</td>
</tr>
<tr>
<td>Run time</td>
<td>6.0 min</td>
</tr>
</tbody>
</table>
RECOMMENDED PROCEDURES

Chromatographic conditions

Chromatograms of DH solutions containing 20 mg of MPS were recorded in the above said conditions by injecting 2 μl into the column. The total time of analysis was found to be less than 6.0 min.

Throughout the study, the suitability of the chromatographic system was monitored by calculating the capacity factor \((k')\), the resolution \((R)\), the selectivity \((\alpha)\) and the peak asymmetry \((A_s)\).

Establishment of calibration curve

Working standard solutions of DH (0.5-15 mg/ml) containing 20 mg of MPS were prepared in methanol. Then 2 μl of the solution was injected and a chromatogram was noted. A typical chromatogram is shown in Fig 1. The ratio of peak areas of DH to that of MPS was calculated and plotted against the concentration of DH to obtain a calibration graph (Fig 2).

Assay procedure for pharmaceutical formulations

An aliquot of the drug obtained by following the procedure described for analysis of pharmaceutical preparations was taken and analyzed. The chromatogram at the above said conditions showed a good resolution between DH and MPS.
RESULTS AND DISCUSSION

For separation of a large number of pharmaceutical compounds OV-101 Stainless steel column has been widely used. This column gave quantitative separation of most of the compounds. Hence, OV-101 stainless steel column was selected for the assay.

Method development

Carrier gas

The nitrogen gas was used as carrier gas throughout the study.

Column

Various analytical columns viz., 10 % OV-101, 5 % OV-101, 3 % OV-101 and 10 % OV-210 were tested for effective separation of DH and MPS. The stationary phase of 3% OV-101 was selected as a column for efficient separation of the component with good peak shapes.

Flow rate

Effects of flow rate were checked by varying it in the ranges of 0.25-2.50 kg/cm²/min. A flow rate of 1.8 kg/cm²/min gave an optimal signal to noise ratio with a reasonable separation time. Hence, a flow rate of 1.8 kg/cm²/min was selected for the study.

Internal standard

After examining the various drugs (amoxyccillin, norfloxacin, piroxicam, diethazine hydrochloride, ceterizine hydrochloride, nortriptyline hydrochloride) for the selection of an internal standard, it was found that the MPS gave the
proper resolution, less time for analysis and good chromatographic behavior compared to others. Hence, MPS was chosen as an internal standard.

**Solvents**

Various solvents like ethanol, butanol, methanol and n-heptane were tried for the selection of solvent. Satisfactory resolution and recoveries were observed with methanol. Hence, it was selected as the extracting and injecting solvent.

**Order of elution**

MPS was eluted first followed by DH.

**Retention times**

The retention times of MPS and DH were observed to be 1.37 and 2.06 min, respectively. The reproducibility of the retention times of DH and MPS was calculated based on the average of five determinations.

**Linearity of detector response**

Linearity and range of the developed method were determined by analyzing 10 different concentrations of the mixed standard solution containing 0.3-18 mg/ml of DH and 20 mg of MPS under the chromatographic conditions (n = 5) mentioned above. The response factor of the standard solutions was calculated. The ratio of peak area of DH to that of MPS was plotted against the concentration of DH to obtain the calibration graph (Fig 2) and was found to be linear over the concentration range of 0.5-15 mg/ml of DH. The data were analyzed by linear regression least-squares method and the corresponding equation is given by \( Y = a + bX \), where \( y \) is the peak area, ‘b’ is the slope, ‘a’ is
the intercept and ‘X’ is the concentration of the analyte. Linear regression least squares fit data are given in Table 1.

Limits of detection and quantification

The limit of detection (LOD) was established at a signal-to-noise ratio (S/N) of 3 while the limit of quantification (LOQ) was calculated at a signal-to-noise ratio (S/N) of 9. The LOD and LOQ were calculated to be 0.171 mg/ml and 0.513 mg/ml, respectively. The results are shown in Table 1.

Suitability of the method

The chromatographic parameters such as resolution, selectivity, capacity factor and peak asymmetry were found to be satisfactory. The values of these parameters are tabulated in Table 2.

Precision and accuracy

By analyzing five replicates of fixed amount of DH, the precision and accuracy of the proposed method was examined. The precision of the method was calculated in terms of the relative standard deviation. Low values of percentage relative standard deviation and percentage error indicated high precision and accuracy of the proposed method. The results are summarized in Table 1.
Interference studies

The interferences from commonly associated excipients in the assay of DH were investigated in order to check the selectivity of the proposed chromatographic method. As evident from Table 3, it was found that the excipients viz., talc, glucose, starch, lactose, sulphate, dextrose, acetate and magnesium stearate did not interfere in the determination of DH in pharmaceutical formulations.

Analysis of pharmaceutical preparation

The applicability of the proposed method was examined by analyzing DH in various pharmaceutical preparations at different concentration levels and the results obtained are shown in Table 4. Low values of relative standard deviation indicated high precision of the proposed method. Recovery values were found to be satisfactory.

CONCLUSIONS

This study showed that the tricyclic antidepressant drug, DH can be precisely and accurately determined in pure and pharmaceutical dosages. The proposed method is simple and requires less time for analysis. System performance parameters revealed that the method is ideal for the assay of DH. High percentage recovery values show that the method is free from interference by the excipients used in the preparations. The utility of the method is well demonstrated by analyzing the pharmaceutical preparations.
REFERENCES


9. W. Misiuk, IL Farmaco. 60 (2005) 61


Fig. 1. A typical chromatogram showing the separation of MPS (20 mg/ml) and DH (10 mg/ml) in pure form.

Fig. 2. Calibration graph for DH.
Table 1. Linear regression least squares fit data for the determination of DH.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>DH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linear dynamic range (mg/ml)</td>
<td>0.5-15</td>
</tr>
<tr>
<td>Regression equation (Y^a)</td>
<td></td>
</tr>
<tr>
<td>Slope (b)</td>
<td>0.41</td>
</tr>
<tr>
<td>Intercept (a)</td>
<td>0.90</td>
</tr>
<tr>
<td>Correlation coefficient, r</td>
<td>0.9992</td>
</tr>
<tr>
<td>% RSD</td>
<td>0.82</td>
</tr>
<tr>
<td>% Error</td>
<td>1.73</td>
</tr>
<tr>
<td>LOD (mg/ml)</td>
<td>0.171</td>
</tr>
<tr>
<td>LOQ (mg/ml)</td>
<td>0.513</td>
</tr>
</tbody>
</table>

Table 2. System performance parameters for DH and MPS.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>MPS</th>
<th>DH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retention time (t_R)</td>
<td>1.37</td>
<td>2.06</td>
</tr>
<tr>
<td>Capacity factor (k')</td>
<td>1.56</td>
<td>7.4</td>
</tr>
<tr>
<td>Peak asymmetry (A_S)</td>
<td>1.42</td>
<td>1.69</td>
</tr>
<tr>
<td>Selectivity factor ((\alpha))</td>
<td></td>
<td>3.64</td>
</tr>
<tr>
<td>Resolution (R)</td>
<td></td>
<td>1.88</td>
</tr>
<tr>
<td>Height equivalent to theoretical plate (H) in mm</td>
<td>120.46</td>
<td>16.37</td>
</tr>
</tbody>
</table>
Table 3. Determination of DH (10 mg) in presence of excipients.

<table>
<thead>
<tr>
<th>Material</th>
<th>Amount, mg</th>
<th>% Recovery of DH ± % RSD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnesium stearate</td>
<td>15</td>
<td>98.8 ± 0.82</td>
</tr>
<tr>
<td>Glucose</td>
<td>25</td>
<td>99.5 ± 0.63</td>
</tr>
<tr>
<td>Lactose</td>
<td>35</td>
<td>100.2 ± 0.92</td>
</tr>
<tr>
<td>Dextrose</td>
<td>30</td>
<td>99.4 ± 0.84</td>
</tr>
<tr>
<td>Starch</td>
<td>20</td>
<td>99.8 ± 0.75</td>
</tr>
<tr>
<td>Gum acacia</td>
<td>25</td>
<td>98.7 ± 1.14</td>
</tr>
<tr>
<td>Talc</td>
<td>30</td>
<td>99.6 ± 0.71</td>
</tr>
<tr>
<td>Sodium alginate</td>
<td>25</td>
<td>100.7 ± 1.23</td>
</tr>
</tbody>
</table>

* Average of five determinations.

Table 4. Analysis of DH in pharmaceutical formulations.

<table>
<thead>
<tr>
<th>Formulations</th>
<th>Label claim (mg)</th>
<th>DH found* (mg)</th>
<th>% RSD</th>
<th>% Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spectra a (Capsule)</td>
<td>10</td>
<td>9.86</td>
<td>0.54</td>
<td>98.60</td>
</tr>
<tr>
<td></td>
<td>25</td>
<td>24.36</td>
<td>0.73</td>
<td>97.44</td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>75.24</td>
<td>0.89</td>
<td>100.32</td>
</tr>
<tr>
<td>Doxedep b (Tablet)</td>
<td>25</td>
<td>24.91</td>
<td>0.63</td>
<td>99.64</td>
</tr>
<tr>
<td></td>
<td>75</td>
<td>74.46</td>
<td>0.78</td>
<td>99.28</td>
</tr>
<tr>
<td>Doxetar c (Capsule)</td>
<td>10</td>
<td>9.81</td>
<td>0.81</td>
<td>98.10</td>
</tr>
<tr>
<td></td>
<td>25</td>
<td>24.55</td>
<td>0.66</td>
<td>98.20</td>
</tr>
</tbody>
</table>

* Average of five determinations.

a Marketed by Ranbaxy Laboratories Ltd. India.

b Marketed by La Pharmaceuticals, India.

c Marketed by Torrent Pharmaceuticals Ltd. India.
Gas chromatographic method for the assay of metaprolol succinate in dosage forms

ABSTRACT

A simple and precise gas chromatographic method for the determination of metaprolol succinate (MPS) in pure and pharmaceutical formulations is proposed. Ibuprofen (IBF) was used as an internal standard. The separation was performed on a 3 % OV-101 (60-80 mesh) stainless steel column of 6 feet length with an internal diameter of 2 mm. Nitrogen gas was used as mobile phase at a flow rate of 1.8 kg/cm²/min. The column temperature was maintained at 250 °C and that of injection port and detector was fixed at 300 °C. The procedure gave a linear response in the concentration range of 1-20 mg/ml with sufficient reproducibility. The method has been applied successfully for the determination of MPS in tablets.

The results of this chapter have been communicated for publication.
General drug profile

The general drug profile of MPS has been given in Chapter 2, Part B, on page number 62.

INTRODUCTION

MPS is a kind of β-adrenaline receptor blocker. It is widely used for the treatment of hypertension, angina, myocardial infarction, arrhythmia, hyperthyroidism and other related diseases [1-3]. It is so sensitive that even a small oral dose of the drug gives sufficient blockade. Since the β-blockers are misused as doping agents in sports, these drugs have been added to the list of forbidden drugs by the International Olympic Committee. It is official in various pharmacopoeia [1-3]. In view of its biological importance, several analytical methods have been directed for quantitative determination of MPS [4-16]. These include gas chromatographic [4,5], high-performance liquid chromatographic [6-10] and spectrophotometric methods [11-16].

The reported gas chromatographic methods [4,5] have many disadvantages viz., tedious sample preparation procedure, require more time for the sample analysis etc. Moreover, the effects of excipients in the determination of MPS have not been studied. The literature survey indicated that no attempt has been made so far to develop a GC method for the determination of MPS employing IBF as an internal standard. In view of this, it was planned to develop precise and accurate GC method for the determination of MPS in bulk and pharmaceutical formulations.
EXPERIMENTAL

Stock solutions

Standard solutions of MPS and IBF were prepared separately by dissolving 1.5 g of MPS and 1.0 g of IBF in methanol and diluting up to the mark in 50 ml volumetric flasks with the same solvent. These solutions were stored in amber colored bottles.

Standard working solutions

Standard working solutions of MPS and IBF were prepared separately in methanol. Aliquots of these solutions were combined and diluted with methanol to obtain solutions containing 1-20 mg/ml of MPS and 20 mg of IBF. Studies on the stability of analytes in standard working solutions showed that there were no decomposition products in the chromatogram during analytical procedure.

Pharmaceutical preparation

Ten tablets of MPS were finely powdered. An amount equivalent to 100 mg of the drug was weighed accurately and transferred into a 100 ml beaker. Using a mechanical stirrer, the powder was completely disintegrated in methanol. The solution was filtered and the filtrate was made up to 50 ml with the same solvent.
Operating conditions

Column : 3% OV-101 (60-80 mesh) packed into a steel column of 6 feet in length and internal diameter of 2 mm

Solvent : Methanol

Internal Standard : Ibuprofen

Carrier gas : Nitrogen

Column temperature : 250 °C

Injection port temperature : 300 °C

Detector temperature : 300 °C

Flow rate : 1.8 kg/cm²/min

Run time : 5 min

RECOMMENDED PROCEDURES

Chromatographic conditions

GC analysis was performed by isocratic elution with nitrogen as carrier gas and keeping the flow rate of 1.8 kg/cm²/min. A volume of 2 µl was injected into the column each time and the chromatogram was recorded by keeping the total chromatographic run time of 5 min.

The suitability of the chromatographic system was monitored by calculating the capacity factor (k¹), resolution (R), selectivity (α) and peak asymmetry (Aₙ).

Establishment of calibration graph

Suitable amounts of aliquots of standard MPS containing 0.75-30 mg/ml were transferred into a series of 5 ml calibrated flasks. To each of these were added 20 mg of IBF, diluted with methanol and mixed well. Then 2 µl of the
solution was injected and a chromatogram was recorded. A typical chromatogram is shown in Fig 1. The ratio of peak areas of MPS to that of IBF were calculated and these values were plotted against the concentration of MPS to obtain a calibration graph (Fig 2).

**Assay procedure for pharmaceutical formulations**

An aliquot of the drug obtained by following the procedure described for analysis of pharmaceutical preparations was taken and analyzed. The chromatogram at the above said chromatographic conditions showed a complete resolution of peaks between MPS and IBF.

**RESULTS AND DISCUSSION**

OV-101 Stainless steel column has been widely used for separation of a large number of pharmaceutical drugs. In the present study, this column gave satisfactory separation of MPS and IBF in methanol.

**Method development**

**Carrier gas**

The nitrogen gas was used as carrier gas throughout the study and found to be ideal for the present work.

**Column**

After evaluating the various stationery phases such as 10% OV-101, 5% OV-101, 3 % OV-101 and 10 % OV-210, the stationery phase of 3% OV-101 was selected for efficient separation of the components with good peak shapes.
Flow rate

Flow rates between 0.5 kg/cm\(^2\)/min to 2.5 kg/cm\(^2\)/min were examined for good chromatographic conditions. A flow rate of 1.8 kg/cm\(^2\)/min was noticed to give an optimal signal to noise ratio with a reasonable separation time.

Internal standard

Various compounds viz., tenofovir, doxepin, amoxycillin, norfloxacin, ceterizine hydrochloride, deflazacort, lercanidipine and IBF were tried. Among these, IBF was selected because of proper resolution, less time for analysis, good chromatographic behavior and peak symmetry.

Selection of Solvent

Methanol was selected as the extracting and injecting solvent because it permitted maximum resolution, lesser period of analysis and high recoveries. Other solvents viz., ethanol, acetonitrile, butanol and n-heptane were tried but satisfactory resolution and recoveries were not observed.

Order of elution

It was observed that MPS was eluted first followed by IBF.

Retention times

The reproducibility of the retention times of MPS and IBF were calculated based on the average of five trials. The retention times of MPS and IBF were observed to be 1.04 min and 1.34 min, respectively.
Linearity of detector response

Linearity and range of the method were determined by analyzing 10 different concentrations of the mixed standard solution containing 0.75-30 mg/ml of MPS and 20 mg of IBF under the chromatographic conditions mentioned above. The response factor of the standard solutions was calculated. The ratio of peak area of MPS to that of IBF was plotted against the concentration of MPS to obtain the calibration graph (Fig 2) and was found to be linear over the concentration range of 1-20 mg/ml. The data were analyzed by linear regression least-squares method and the corresponding equation is given by Y = a + bX, where Y is the ratio of peak area, ‘b’ is the slope, ‘a’ is the intercept and ‘X’ is the concentration of the analyte. Linear regression least squares fit data are given in Table 1.

Limits of detection and quantification

The limit of detection (LOD) was established at a signal-to-noise ratio (S/N) of 3 while the limit of quantification (LOQ) was calculated at a signal-to-noise ratio (S/N) of 10. The LOD and LOQ were calculated to be 0.367 mg/ml and 1.102 mg/ml, respectively. The results are shown in Table 1.

Suitability of the method

The chromatographic parameters such as resolution, selectivity and peak asymmetry were noticed to be satisfactory for the selected drugs and the corresponding results are shown in Table 2.
**Precision and accuracy**

By analyzing five replicates of fixed amount of MPS, the precision and accuracy of the proposed method were tested. The precision of the method was calculated in terms of the relative standard deviation while accuracy was expressed in terms of % error. Low values of percentage relative standard deviation and percentage error indicated high precision and accuracy of the proposed method, respectively (Table 1).

**Interference studies**

In order to examine the selectivity of the method, the effects of commonly associated excipients in the assay of MPS were investigated. It was found that the excipients *viz.*, talc, glucose, starch, lactose, sulphate, dextrose, acetate and magnesium stearate did not interfere in the determination of MPS in pharmaceutical formulations (Table 3).

**Application**

**Analysis of pharmaceutical formulations**

The proposed method was applied to the assay of MPS in pharmaceutical preparations at different concentration levels and the results obtained are shown in Table 4. High reproducibility of the proposed method was evident from low values of relative standard deviation. The % recovery values were observed to be in the range of 97.8-100.2.
CONCLUSIONS

Using the described gas chromatographic method, MPS can be determined in pharmaceutical formulations quite accurately within 5 min. Excipients did not interfere in the proposed method. Hence, the proposed method could be adopted for routine quality control by pharmaceutical industries.
REFERENCES


Fig. 1. A typical chromatogram showing the separation of MPS (15 mg/ml) and IBF (20 mg/ml) in pure form.
Fig. 2. Calibration graph for MPS.
Table 1. Linear regression least squares fit data for the determination of MPS.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linear dynamic range (mg/ml)</td>
<td>1-20</td>
</tr>
<tr>
<td>Regression equation ($Y^a$)</td>
<td></td>
</tr>
<tr>
<td>Slope (b)</td>
<td>0.4728</td>
</tr>
<tr>
<td>Intercept (a)</td>
<td>0.3614</td>
</tr>
<tr>
<td>Correlation coefficient, r</td>
<td>0.9977</td>
</tr>
<tr>
<td>% RSD</td>
<td>1.46</td>
</tr>
<tr>
<td>% Error</td>
<td>1.82</td>
</tr>
<tr>
<td>LOQ (mg/ml)</td>
<td>0.367</td>
</tr>
<tr>
<td>LOD (mg/ml)</td>
<td>1.102</td>
</tr>
</tbody>
</table>

Table 2. System performance parameters of MPS and IBF.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>MPS</th>
<th>IBF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retention time ($t_R$)</td>
<td>1.04</td>
<td>1.34</td>
</tr>
<tr>
<td>Capacity factor ($k^1$)</td>
<td>1.44</td>
<td>7.1</td>
</tr>
<tr>
<td>Peak asymmetry ($A_s$)</td>
<td>1.38</td>
<td>1.55</td>
</tr>
<tr>
<td>Selectivity factor ($\alpha$)</td>
<td>3.59</td>
<td></td>
</tr>
<tr>
<td>Resolution ($R$)</td>
<td></td>
<td>1.72</td>
</tr>
<tr>
<td>Height equivalent to the theoretical plate ($H$) in mm</td>
<td>116.32</td>
<td>15.86</td>
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</table>
Table 3. Determination of MPS (10 mg) in presence of excipients.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Amount, mg</th>
<th>% Recovery of MPS ± % RSD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnesium stearate</td>
<td>30</td>
<td>99.6 ± 0.65</td>
</tr>
<tr>
<td>Glucose</td>
<td>35</td>
<td>98.9 ± 0.64</td>
</tr>
<tr>
<td>Lactose</td>
<td>35</td>
<td>100.2 ± 0.89</td>
</tr>
<tr>
<td>Dextrose</td>
<td>30</td>
<td>99.8 ± 0.91</td>
</tr>
<tr>
<td>Starch</td>
<td>30</td>
<td>98.7 ± 1.24</td>
</tr>
<tr>
<td>Gum acacia</td>
<td>35</td>
<td>100.5 ± 0.78</td>
</tr>
<tr>
<td>Talc</td>
<td>30</td>
<td>99.1 ± 0.95</td>
</tr>
<tr>
<td>Sodium alginate</td>
<td>25</td>
<td>99.2 ± 1.41</td>
</tr>
</tbody>
</table>

* Average of five determinations.

Table 4. Analysis of MPS in pharmaceutical formulations.

<table>
<thead>
<tr>
<th>MPS Tablet</th>
<th>Labeled, mg</th>
<th>MPS found*, mg/tablet</th>
<th>% RSD</th>
<th>% Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metolar*</td>
<td>25</td>
<td>24.8</td>
<td>0.82</td>
<td>99.2</td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>48.9</td>
<td>0.68</td>
<td>97.8</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>100.2</td>
<td>1.14</td>
<td>100.2</td>
</tr>
<tr>
<td>Seloken-XLb*</td>
<td>25</td>
<td>24.7</td>
<td>0.75</td>
<td>98.8</td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>49.6</td>
<td>0.92</td>
<td>99.2</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>99.8</td>
<td>0.77</td>
<td>99.8</td>
</tr>
</tbody>
</table>

* Average of five determinations.

Marketed by: * Cipla pharmaceuticals Ltd.

  b Astra Zeneca, India, Ltd.