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Research Article

Quantitative Determination of Metformin Hydrochloride in Tablet Formulation Containing Croscarmellose Sodium as Disintegrant by HPLC and UV Spectrophotometry

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Abstract

Purpose: *To develop and validate a suitable method for the assay of metformin hydrochloride (HCl) in tablets containing croscarmellose sodium as an additive.*
Methods: *Methanol and ethanol (99%) were assessed as solvents for sample preparation for the assay of metformin HCl in tablets containing croscarmellose sodium by high performance liquid chromatography (HPLC) and ultra violet spectrophotometric (UV) methods. The proposed method was subjected to validation tests.*
Results: *Recovery of metformin HCl from the placebo-spiked sample was 95.1 to 96.9 % as per BP and USP methods compared with 99.3 to 100.8 % when analyzed by the proposed method. The use of methanol and ethanol as solvents resolved the problem of retention of metformin HCl by croscarmellose sodium in solution during the preparation of sample solution.*
Conclusion: *The modified UV and HPLC methods are suitable for the determination of metformin HCl in tablets both in the presence and absence of croscarmellose sodium. The method is specific, precise, accurate, robust, rugged and gives a linear response for the quantitative estimation of metformin HCl in tablet formulation.*

Keywords: *Tablets; Metformin HCl assay; Croscarmellose sodium; Ethanol; Methanol; HPLC, UV*

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INTRODUCTION

Metformin HCl is a biguanidine class of anti-diabetic drug prescribed orally for the treatment of non-insulin-dependent diabetes mellitus [1-4]. The assay of metformin HCl in immediate release tablets is usually carried out by UV spectrophotometry as per British Pharmacopoeia (BP) and United States Pharmacopoeia (USP) while HPLC method of assay has been given in the USP monograph for extended release metformin tablets [5-6]. Some methods have been reported in the literature for the estimation of metformin HCl in the presence of other drugs in formulations [7-19].

In the assay methods of BP and USP for immediate release metformin tablet, water is used for sample preparation while 10 % acetonitrile is used for sample preparation in the case of the assay of extended release metformin tablets by the USP method. These methods work well for metformin tablets which do not contain croscarmellose sodium as a disintegrant but are unsatisfactory for the assay of metformin HCl in metformin tablets containing croscarmellose sodium as a disintegrant due to poor recovery of metformin during the preparation of sample solution. Many of the commercial tablets of metformin HCl contain croscarmellose sodium as a disintegrant.

It has been reported in the literature that when metformin HCl is spiked to an aqueous solution containing croscarmellose sodium, a strong charge interaction occurs between metformin HCl and croscarmellose sodium. This charge interaction results in the retention of metformin in croscarmellose sodium leading to lower drug recovery during the preparation of the sample solution.

In a previous study, arginine was selected to compete with metformin HCl for the binding sites on croscarmellose sodium. The report states that because of the competition and stronger interaction between arginine and croscarmellose sodium, compared to the interaction between metformin and croscarmellose sodium, complete recovery of metformin was achieved [20].

Therefore, the objective of the present study was to replace the solvents of the BP and USP methods with appropriate solvents in which croscarmellose sodium is poorly soluble in order to obtain satisfactory recovery of metformin HCl.

EXPERIMENTAL

Reagents and materials

The working standard of Metformin HCl (99.1% pure) was obtained from Micro Labs Ltd, India. The 1-heptane sulphonic acid sodium salt used was of analytical reagent (AR) grade (Spectrochem, India) Sodium chloride and ortho-phosporic acid were of general purpose (GR) grade (Merck, India), ethanol (99 % v/v, GR grade, Changshu Yangyuan Chemicals, China), acetonitrile and methanol (HPLC grade, Merck, India) were also used. Water purified with Millipore water system (Elix 10 C model) was used for the preparation of buffer. Polytetra-fluoroethylene (PTFE) membrane filters (0.45 µ, syringe filter – 25 mm GD/X- Whatman) were used for the filtration of solutions. Cellulose acetate filter (0.45 µ, Sartorium, Sedim) was used for the filtration of the mobile phase.

UV Spectrophotometer

A Shimadzu UV-visible spectrophotometer (model UV-1700 PharmaSpec) was used for UV spectrophotometric experiments.

Chromatographic conditions

A Waters high performance liquid chromatographic (HPLC) system equipped with a 2695 solvent delivery system, Waters auto injector, thermostatted column

compartment and Waters 2998 photo diode array detector was used for the experiment. The samples were analysed using a Waters column (µBondapak C-18 column of 300mm x 3.9mm i.d.,10 µ particle size). A mixture of buffer and acetonitrile in the ratio of 90:10 (v/v) was used as the mobile phase. The buffer for the mobile phase was prepared by dissolving 1.0 g of each of 1-heptane sulphonic acid sodium salt and sodium chloride in 1800 mL of water, adjusting the pH to 3.85 ± 0.05 using 0.06M phosphoric acid and making up the volume to 2000 mL with water. The buffer and acetonitrile mixture was degassed by sonication and filtered through 0.45 µ cellulose acetate membrane filter.

Preparation of standard solutions for the proposed method

Preparation of standard metformin HCl solution using ethanol (99 %v/v) (Solution 1)

About 100 mg of metformin HCl powder was accurately weighed into a dry 100 mL volumetric flask and sonicated with 70 mL of ethanol (99 %v/v) and made up to 100 mL with ethanol (99 %v/v) and filtered through a 0.45 µ PTFE membrane filter. The filtrate (10 mL) was diluted to 100 mL with water (standard solution for HPLC method containing 100 µg/mL of metformin HCl). This standard solution (10 mL) was diluted to 100 mL using water to obtain the standard solution for UV spectrophotometric determination (10 µg/mL of metformin HCl).

Preparation of standard metformin HCl solution using methanol (Solution 2)

Solution 2 was prepared exactly like Solution 1 but using methanol instead of ethanol (99 %v/v).

Preparation of standard solutions for BP/USP methods

Preparation of standard solution for UV spectrophotometric estimation as per BP/USP method (Solution 3)

About 10 mg of metformin HCl powder was accurately weighed, dissolved in 70 mL of water by sonication and made up to 100 mL with water. This solution (10 mL) was diluted to 100 mL with water (10 µg/mL of metformin HCl).

Preparation of standard metformin HCl solution for HPLC method of assay as per USP (Solution 4)

About 12.5 mg of metformin HCl powder was accurately weighed and dissolved in 70 mL of 1.25% v/v solution of acetonitrile in water by sonication. The volume was made up to 100 mL with the same diluent. This solution (10 mL) was diluted to 100 mL with the diluent (12.5 µg/mL of metformin HCl).

Preparation of tablet sample solutions for proposed method

Preparation of tablet sample solution using ethanol (99% v/v) for UV spectrophotometric and HPLC determinations (Solutions 5 and 6)

Twenty metformin HCl tablets (containing croscarmellose sodium as one of the additives) were powdered and the tablet powder equivalent to about 100 mg of metformin HCl was accurately weighed into a dry 100 mL volumetric flask. About 70 mL of ethanol (99% v/v) was added, sonicated for 15 min with intermittent shaking and the volume was made up to 100 mL with ethanol (99 %v/v). This solution was filtered through a 0.45 µ PTFE membrane filter. The filtrate (10 mL) was diluted to 100 mL with water to get a solution of 100 µg/mL of metformin HCl (Solution 5 for HPLC method). Further, 10 mL of Solution 5 was diluted to 100 mL with water to obtain a solution containing 10

µg/mL of metformin HCl (Solution 6 for UV spectrophotometric method).

Preparation of Tablet Sample Solution using methanol as diluent for UV spectrophotometric and HPLC determinations (Solutions 7 and 8)

Solutions 7 and 8 were prepared exactly like Solutions 5 and 6 but using methanol instead of ethanol (99% v/v).

Preparation of tablet sample solution as per BP/USP method

Preparation of sample solution for UV spectrophotometric method as per BP/USP (Solution 9)

Twenty metformin HCl tablets (containing croscarmellose sodium as one of the additives) were powdered and tablet powder equivalent to about 100 mg of metformin HCl was accurately weighed and sonicated with 70 mL of water for 15 min with intermittent shaking. The volume was made up to 100 mL with water and the solution filtered through a 0.45 µ PTFE membrane filter. The filtrate (10 mL) was diluted to 100 mL with water. Further, 10 mL of this solution was diluted to 100 mL using water (10 µg/mL of metformin HCl).

Preparation of sample solution for HPLC Method as per USP (Solution 10)

Ten metformin HCl tablets (containing croscarmellose sodium as one of the additives) were powdered and tablet powder equivalent to about 500 mg of metformin HCl was accurately weighed into a homogenization vessel. A solution of 10% acetonitrile (500 mL) was added, alternatively homogenized and soaked until the sample was completely homogenized. The solution was then filtered through a 0.45 µ PTFE membrane filter. The filtrate (25 mL) was diluted to 200 mL with water in a 200 mL volumetric flask. Out of this, 10 mL of the solution was diluted to 100 mL in a 100 mL volumetric flask using 1.25 % acetonitrile as diluent in water to obtain a concentration of 12.5 µg/mL of metformin HCl.

Preparation of Solution of Metformin HCl in the presence of placebo for proposed method

Preparation of solution as per proposed method using ethanol (99 %v/v) as diluent for UV spectrophotometric and HPLC determination (Solutions 11 and 12)

Metformin HCl (100 mg) and 100 mg of placebo powder containing croscarmellose sodium 5 mg, povidone 5 mg, silicon dioxide 1 mg, talc 1 mg, magnesium stearate 0.2 mg, lactose 12.8 mg, microcrystalline cellulose 15 mg and maize starch 10 mg
was accurately weighed into a dry 100 mL volumetric flask. About 70 mL of ethanol (99 %v/v) was added and sonicated for 15 min with intermittent shaking. The volume was made up to 100 mL with ethanol (99 %v/v) and filtered through a 0.45 µ PTFE membrane filter. The filtrate (10 mL) was diluted to 100 mL with water to obtain a solution of 100 µg/mL of metformin HCl (Solution 11 for HPLC method). Further, 10 mL of Solution 11 was diluted to 100 mL with water to obtain a solution containing 10 µg/mL of metformin HCl (Solution 12 for UV spectrophotometric method).

Preparation of solution as per proposed method using methanol as diluent for UV spectrophotometric and HPLC estimation (Solution 13 and 14)

Solutions 13 and 14 were prepared using procedures similar to to those for Solutions 11 and 12, respectively, except that methanol was used instead of ethanol (99 %v/v) for the preparation.

Preparation of solution of metformin HCl in presence of placebo for BP/USP methods

Preparation of solution for UV spectrophotometric method as per BP/USP (Solution 15)

Metformin HCl (100 mg) and 100 mg of placebo powder containing croscarmellose sodium 5 mg, povidone 5 mg, silicon dioxide 1 mg, talc 1 mg, magnesium stearate 0.2 mg, lactose 12.8 mg, microcrystalline cellulose 15 mg and maize starch 10 mg was accurately weighed into a dry 100 mL volumetric flask. Water (70 mL) was added and sonicated for 15 min with intermittent shaking. The volume was made up to 100 mL with water and filtered through a 0.45 µ PTFE membrane filter. This filtrate (10 mL) was diluted to 100 mL with water and 10 mL of this solution was further diluted to 100 mL with water to obtain a concentration of 10 µg/mL of metformin HCl (Solution 15).

Preparation of solution as per USP HPLC method (Solution 16)

Metformin HCl (500 mg) and 500 mg of placebo powder containing croscarmellose sodium (50mg) as one of the additives were accurately weighed into a homogenization vessel. A solution of 10 % acetonitrile (500 mL) was added, alternatively homogenized and soaked until the sample was completely homogenized. The solution was then filtered through a 0.45 µ PTFE membrane filter. The filtrate (25 mL) was diluted to 200 mL with water and 10 mL of this solution was further diluted to 100 mL using a diluent of 1.25 % acetonitrile in water to obtain a concentration of 12.5 µg/mL of metformin HCl (Solution 16)

Preparation of solution of metformin HCl in presence of croscarmellose sodium for proposed method

Preparation of solution of metformin HCl in croscarmellose sodium by proposed method using ethanol as diluent for UV spectrophotometric and HPLC estimation (Solutions 17-26)

About 100 mg of metformin HCl substance was transferred into each of 5 different 100 mL volumetric flasks. To the above 5 volumetric flasks different quantities (5 mg, 10 mg, 25 mg, 50 mg, and 100 mg) of croscarmellose sodium was added. To the each of the flask, 70 mL of ethanol (99% v/v) was added and sonicated for 15 minutes with intermittent shaking. The volume of each of the flask was made up to 100 mL with ethanol and filtered through a 0.45 µ PTFE membrane filter. The filtrate (10 mL) of each of the 5 solution was diluted to 100 mL with water in separate seven 100 mL volumetric flasks to obtain a concentration of 100 µg/mL of metformin HCl. (These solutions 17 to 21 were used for the estimation of metformin HCl by HPLC method). An aliquot (10 mL) of each of solutions 17 to 21 was diluted to 100 mL in 5 separate volumetric flasks with water to obtain a concentration of 10 µg/mL of metformin HCl. (The resulting solutions, 22 to 26, were used for the determination of metformin HCl by UV spectrophotometric method).

Preparation of solution of metformin HCl in croscarmellose sodium by proposed method using methanol as diluent for UV spectrophotometric and HPLC estimation (Solutions 27 to 36)

Solutions 27 to 36 were prepared as described for Solutions 17 to 26 except that methanol was used instead of ethanol.

Preparation of solution of metformin HCl in presence of croscarmellose sodium for BP/USP methods

Preparation of solution of metformin HCl in croscarmellose sodium by UV spectro-photometric method as per BP / USP (Solutions 37- 41)

About 100 mg of metformin HCl substance was transferred into each of 5 different 100 mL volumetric flasks. To the above 5 volumetric flasks different quantities (5 mg, 10 mg, 25 mg, 50 mg, and 100 mg) of croscarmellose sodium was added. To the each of the flask 70 mL of water was added and sonicated for 15 minutes with intermittent shaking. The volume of each of the flask was made up to 100 mL with water, mixed well, and filtered through a 0.45 µ PTFE membrane filter. The filtrate (10 mL) of each of the 5 solutions was diluted to 100 mL with water and 10 mL of each of the solution was further diluted to 100 mL using water to obtain a concentration of 10 µg/mL of metformin HCl for each solution.

Preparation of solution of metformin HCl in croscarmellose sodium by HPLC method as per USP (Solutions 42- 46)

About 500 mg of metformin HCl substance was transferred into each of 5 homogenization vessels. To the above 5 vessels different quantities (25 mg, 50 mg, 125 mg, 250 mg, and 500 mg) of croscarmellose sodium was added. To the each of the vessels, 500 mL of 10 % acetonitrile was added, alternatively homogenized and soaked until the sample was completely homogenized. Each of the solution was then filtered through 0.45 µ PTFE membrane filter. The filtrate (25 mL) of each of the 5 solutions was diluted to 200 mL with water and 10 mL of each solution was further diluted to 100 mL using diluent of 1.25% v/v acetonitrile in water to obtain a concentration of 12.5 µg/mL of metformin HCl in each solution.

UV spectrophotometric estimation

The absorbance of solutions prepared for UV spectrophotometric determination was recorded at 232 nm using water as blank. The content of metformin HCl was calculated by external standard method. In this method, the reference analyte, at the same concentration as that of the test analyte was chromatographed. The response of the reference analyte, such as AUC value, was used for the quantitative determination of the test analyte.

Chromatographic parameters

For HPLC analysis, a flow rate of 1.0 mL/minute and detection wavelength of 218 nm was used. The sample injection volume was 20 µL and the column was maintained at a temperature of 30 ℃. The run time for each injection was 10 min.

Method validation

The UV spectrophotometric and HPLC methods were validated for specificity, linearity and range, precision, accuracy, robustness and solution stability according to USP and ICH guidelines.

Specificity

The specificity of the method was evaluated by spiking metformin hydrochloride into the placebo containing croscarmellose sodium as an additive and checking the interference of the placebo in the assay of metformin HCl.
The stability indicating nature of the HPLC method was evaluated by stress studies on drug substance, placebo and formulation using the stress agents of acid, alkali and oxidation with hydrogen peroxide. The thermal degradation was carried out by heating the drug substance, placebo and formulation and photo degradation was performed by exposing the drug substance, placebo and formulation to UV light. The spectral purity of the metformin peak was

been evaluated using Empower software, version 2.

Linearity and range

The linearity and range of the method was established by recording the response of standard preparation at 5 different concentrations prepared in the range of 50 to 150 % of median concentration. The linear regression analysis of the data was done by the the method of least squares. The correlation coefficient values have been reported.

Precision

The precision of the method was determined by measuring the repeatability (intra-day precision) and the intermediate precision (inter-day precision). Precision was calculated from six determinations of the test metformin HCl tablets on same day (intra-day precision) and on two different days (inter-day precision). The % RSD of the content of metformin HCl was calculated.

Accuracy

The accuracy of the method was determined by checking the recovery of metformin HCl from placebo spiked with metformin HCl. Metformin HCl was spiked at five different concentration levels (i.e., 50 to 150 % of median concentration) into placebo containing croscarmellose sodium as an additive. The % recovery range and % RSD at each level was calculated.

Robustness

Robustness was established by varying the chromatographic conditions with respect to flow rate, pH of buffer, % of organic modifier and wavelength. Standard and sample solutions were injected and % metformin content was calculated under these modified conditions.

Solution stability

The solution stability of the standard and sample solutions was studied for 24 hours at ambient temperature in the lab. The percentage difference of peak area / absorbance of standard solution and sample solution were recorded.

Statistical analysis

The % RSD value and linear regression analysis by the method of least squares0 were calculated using Microsoft Excel 2003 application.

RESULTS

The results of % recovery of metformin HCl from a matrix of croscarmellose sodium spiked with metformin HCl in the ratio of 1:1 are presented in Table 1 while % recovery from metformin HCl and croscarmellose sodium mixtures by USP/BP methods and the proposed method are given in Table 2. Table 3 presents the results of % recovery from the test tablets.

The proposed UV and HPLC methods were validated and the results of method validation are presented in Table 4. The validation data, including specificity, linearity, range, accuracy, precision, robustness and solution stability were all within the acceptance criteria for both UV and HPLC method.

DISCUSSION

The recovery of metformin HCl from a mixture of metformin HCl and croscarmellose sodium varied significantly with the solvents used and is > 99 % for both methanol and ethanol. Recovery is almost the same for both UV spectrophotometry and HPLC methods using various solvents. Since the croscarmellose sodium used as an additive in tablet formulations is very poorly soluble in methanol and ethanol, metformin HCl was not retained in solution due to charge interaction; hence, recovery was high when methanol and ethanol were used for sample preparation. Croscarmellose sodium was

Table 1: Recovery of metformin HCl from spiked croscarmellose sodium with various solvents (n = 6)

Diluent	% Recovery of metformin HCl [a] (mean ± SD)	
	UV method	***HPLC method***
0.1N Hydrochloric acid	78.8 ± 0.5	80.1 ± 0.5
pH 4.5 Acetate Buffer	92.3 ± 0.7	93.5 ± 0.3
pH 6.8 Phosphate Buffer	95.1 ± 0.3	96.3 ± 0.7
Water	70.9 ± 0.6	71.3 ± 0.5
Methanol	99.8 ± 0.3	99.4 ± 0.4
Ethanol	100.1 ± 0.5	99.6 ± 0.4
Acetonitrile	-[b]	-[b]
Water : Acetonitrile (1:1)	77.4 ± 0.2	78.1 ± 0.3
Water : Methanol (1:1)	74.1 ± 0.6	76.1 ± 0.5
Water : Ethanol (1:1)	79.8 ± 0.5	79.1 ± 0.6

[a] *Recovery from Croscarmellose sodium spiked with Metformin HCl (1:1).* [b]*Note: No recovery because metformin hydrochloride is poorly soluble in acetonitrile*

Table 2: Recovery of metformin HCl from metformin HCl spiked with different ratios of croscarmellose sodium (n = 6)

Ratio of metformin hydrochloride to croscarmellose sodium in spiked sample	% Recovery of metformin HCl by UV and HPLC methods (mean ± SD) [a]					
	BP/USP Method		**Proposed method**			
	Water (as diluent)	***10.0% Acetonitrile as diluent***	***Methanol (as diluent)***		***Ethanol (as diluent)***	
	UV method	HPLC method	UV method	HPLC method	UV method	HPLC method
1 : 0.05	96.7 ± 0.3	96.1 ± 0.5	99.8 ± 0.3	99.9 ± 0.7	99.9 ± 0.6	100.1 ± 0.7
1 : 0.10	95.4 ± 0.5	95.2 ± 0.4	99.4 ± 0.5	100.3 ± 0.4	99.7 ± 0.5	100.3 ± 0.5
1 : 0.25	91.5 ± 0.5	93.3 ± 0.7	100.1 ± 0.6	100.2 ± 0.7	100.6 ± 0.4	99.5 ± 0.5
1 : 0.50	84.6 ± 0.7	84.9 ± 0.8	100.3 ± 0.9	99.8 ± 0.6	99.8 ± 0.4	99.8 ± 0.5
1 : 1.00	72.2 ± 0.7	75.5 ± 0.7	99.7 ± 0.8	100.5 ± 0.5	100.1 ± 0.6	100.5 ± 0.2

Table 3: Recovery of metformin HCl from test tablet

Diluent	***UV method*** **(mean ± SD)**	***HPLC method*** **(mean ± SD)**
Test tablets[a]		
BP/USP diluent [c]	95.1 ± 0.5	96.6 ± 0.5
Proposed diluent (methanol)	100.3 ± 0.5	99.2 ± 0.5
Proposed diluent (ethanol)	99.5 ± 0.4	100.4 ± 0.3
Spiked placebo sample[b]		
BP/USP diluent [c]	95.1 ± 0.4	96.9 ± 0.2
Proposed diluent (methanol)	100.6 ± 0.4	99.3 ± 0.4
Proposed diluent (ethanol)	100.8 ± 0.4	99.6 ± 0.2

[a] *Each (1000 mg) tablet contains 50 mg of Croscarmellose Sodium, 500 mg of Metformin HCl and 450 mg of other excipients;* [b] *Placebo powder (100mg) contains 10 mg of Croscarmellose Sodium and 90 mg of other excipients;* [c] *Water as diluent for UV method and 10.0 % acetonitrile in water as diluent for HPLC method*

Table 4: Method validation data for proposed UV and HPLC methods

Parameter	UV method		HPLC method		Acceptance criteria
	Methanol (as diluent)	***Ethanol (as diluent)***	***Methanol (as diluent)***	***Ethanol (as diluent)***	
(i) Specificity	No interference was found	No interference was found	No interference was found / Peak purity passes	No interference was found / Peak purity passes	The interference should be NIL/ Peak purity should pass.
(ii) Linearity	R =0.9999	R = 0.9998	R = 0.9998	R = 0.9999	>0.9990
(iii) Range	5 to 15 µg/mL	5 to 15 µg/mL	50 to 150 µg/mL	50 to 150 µg/mL	-
(iv) Accuracy (% Recovery)	99.3 to 100.6 %	99.6 to 100.3 %	99.2 to 100.6 %	99.8 to 100.9%	98.0 – 102.0 %
(v) Precision (%RSD)					
-Repeatability	0.6 %	0.4 %	0.5 %	0.6%	≤ 2.0%
-Intermediate precision	0.5 %	0.6 %	0.4 %	0.3%	
(vi) Robustness (% Assay)	Change in detection wavelength		Change in flow rate, detection wavelength, pH of buffer and mobile phase composition		
	99.5 to 100.2%	99.3 to 100.4%	99.1 to 99.8%	99.3 to 100.7%	98.0 – 102.0 %
(vii) Solution stability	% Difference in absorbance /AUC values in comparison to the initial value				

Time	Standard	Sample	Standard	Sample	Standard	Sample	Standard	Sample	
After 6 h	0.5	0.6	0.4	0.3	0.2	0.4	0.3	0.3	≤ 2.0 %
After 12 h	0.2	0.3	0.2	0.4	0.6	0.2	0.5	0.4	
After 18 h	0.6	0.4	0.6	0.7	0.3	0.7	0.2	0.2	
After 24 h	0.3	0.7	0.5	0.8	0.4	0.3	0.6	0.2	

almost totally removed by filtration in the first step of sample preparation in the proposed method, thereby preventing charge interaction.

Recovery of metformin decreased with increase in the level of croscarmellose sodium in the spiked mixture when water and 10 % acetonitrile (as per BP and USP) were used. The % recovery fell to about 75 % with these solvents when the ratio of metformin HCl to croscarmellose was 1:1 whereas for the proposed methods the solvents used (methanol and ethanol) were able to recover about 100 % from the 1:1 mixture. Thus, recovery of metformin HCl by the solvents used in the proposed method is independent of the level of croscarmellose sodium in the sample matrix up to a ratio of 1:1.

It is also evident from the data obtained that the solvents used in the proposed method were able to recover about 99 to 100 % of metformin HCl from tablet samples and spiked placebo samples. Thus, the proposed method which utilized methanol and ethanol (99 %) as solvents stands validated in terms of accuracy, linearity, specificity, range, robustness and stability of solution.

CONCLUSION

The developed method which incorporates a change in the solvent used in the BP/USP

methods for the initial dilution of the tablet samples would lead to accurate quantification of metformin HCl in the presence of croscarmellose sodium. The developed method was successfully validated and should be used for the assay of metformin hydrochloride in metformin HCl tablets containing croscarmellose sodium as an additive.

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