Research Article

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Method Development and Validation of Magaldrate and simethicone by RP HPLC Method

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ABSTRACT

A simple, accurate, economical, rapid, selective, reverse phase high performance liquid chromatography (RP-HPLC) was developed for simultaneous estimation of Magaldrate andSimethicone in its bulk dosage form. The separation was carried out using a mobile phase of Triethylamine buffer and acetonitrile(50:50) pumped at a flow rate of 1 ml/min along with 227nm as a UV detection wavelength. The stationary phase used wasInertsil ODS 3V column,C18(150x4.6 ID) 5µm. Magaldrate andSimethicone were eluted at a retention time of about 2.483 min for Magaldrate and 3.710 min for Simethicone. The method was developed and validated as per ICH guidelines by considering the parameters such as precision, accuracy, linearity, specificity, robustness and ruggedness. Linearity was 0.9963 for Magaldrate and 0.9989 for Simethicone.the %RSD was less than 2%. The % recovery of Magaldrate was100.17 and Simethicone was 100.61. The developed RP-HPLC method can be used for routine analysis of Magaldrate andSimethicone in combinational dosage form.

Keywords: RP-HPLC, method development, Validation, Magaldrate, Simethicone

INTRODUCTION

Magaldrate is an antacid drug used for the treatment of esophagitis, duodenal and gastric ulcers, and gastroesophageal reflux.Magaldrate is a hydroxymagnesium aluminate complex that is converted rapidly by gastric acid into $Mg(OH)_2$ and $Al(OH)_3$, which are absorbed poorly and thus provide a sustained antacid effect.[1-5]Magaldrate may negatively influence drugs like tetracyclines, benzodiazepines, and indomethacin. High doses or prolonged usage may lead to an increment of defecation and a reduction in feces consistence. In some cases it can alter the functionality of the gastrointestinal tract, occasionally provoking constipation or diarrhea.

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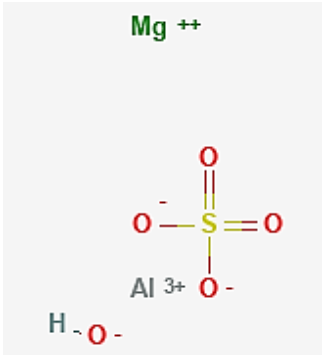


Fig.1: Chemical structure of Magaldrate

Simethicone is a silicon based surfactant that decreases the surface tension of gastrointestinal gas bubbles to facilitate their elimination. It has a favourable safety profile as it is not systemically absorbed. Simethicone has been in use since the 1940s but was granted FDA approval in 1952. Simethicone is indicated for the treatment of bloating, pressure, and cramps caused by gas.[6-10] Simethicone is also used as part of bowel preparation for colonoscopies. Simethicone is a surfactant that decreases the surface tension of gas bubbles in the gastrointestinal tract, more easily allowing gas to exit the body.

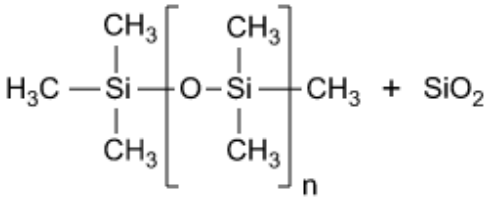


Fig. 2: Chemical structure of Simethicone

Validation of Analytical Methods

Method validation, according to the United States Pharmacopeia (USP), is performed to ensure that an analytical methodology is accurate, specific, reproducible, and rugged over the specified range that an analyte will be analyzed. Regulated laboratories must perform method validation in order to be in compliance with FDA regulations.[11-13] In a 1987 guideline (Guideline for Submitting Samples and Analytical Data for Methods Validation), the FDA designated the specifications in the current edition of the USP as those legally recognized when determining compliance with the Federal Food, Drug and Cosmetic Act can be referred to as the "eight steps of method validation"

EXPERIMENTAL

Table. 1: Optimized Conditions

EQUIPMENTS	SOURCE
High Pressure Liquid Chromatography (HPLC)	Shimadzu(LC 20 AT VP)
Chromatographic data software	Spin chrome (LC SOLUTIONS)
Column	Inertsil ODS 3V(250x4.6mm) 5µm
Detector	UV
Injector	Automated
Electronic Balance	Scaletec
Sonicator	Band Line Sonerex
p^H Meter	Digisun

Method Validation

The analytical procedure refers to the way of performing the analysis. It should describe in detail the steps necessary to perform each analytical test. This may include but is not limited to: the sample, the reference standard and the reagents preparations, use of the apparatus, generation of the calibration curve, use of the formulae for the calculation, etc. The described method extensively validated in terms of specificity, system suitability, linearity, accuracy, precision, limit of detection, limit of quantification and robustness.

Preparation of Standard solution

About 10 mg of Magaldrate and Simethicone were weighed into volumetric flask of 100ml, to this 50 mL solvent was added, sonicated and subjected to volume make up to the mark on the volumetric flask with the solvent.

Preparation of sample solution

Weigh about 10 mg of sample and transfer in to 100ml volumetric flask, add 50ml of mobile phase sonicated and subjected to volume make up with the solvent.

Dilutions

Necessary dilutions are made from standard stock solutions(1ml of stock solution to 10ml) to get the concentration range of 10 µg/mL of Magaldrateand 10 µg/mL of Simethicone.

RESULTS

Table. 2: Method precision results for Magaldrate and Simethicone.

Injection	MAGALDRATE		SIMETHICONE	
	Rt	Area	Rt	Area
1	2.397	3898.811	5.630	591.352
2	2.403	3954.691	5.650	605.193
3	2.393	3996.327	5.603	610.259
4	2.387	3941.128	5.597	620.470
5	2.347	3902.778	5.523	610.067
6	2.403	3948.922	5.650	614.702
Average	2.3883	3940.443	5.609	608.674
SD	0.0212	36.195	0.048	9.921
%RSD	**0.89**	**0.92**	**0.85**	**1.63**

RESULT

The %RSD of 6 determinations of Magaldrate and Simethicone for System precision was in the limit i.e,< 2.0%.

Linearity and range

Preparation of standard stock solution

Standard stock solutions of magaldrateand simethicone were prepared by dissolving 10 mg of magaldrate and 10 mg of simethicone in 100 mL of mobile phase. After that filter it and sonicated for 5 min further dilutions were given in the Table 3.

Table. 3: Linearity Preparations.

Preparations	Volume from standard stock	Volume(with mobile phase)	Concentration Magaldrate	Simethicone
Preparation 1	0.5	10	50	50
Preparation 2	0.75	10	75	75
Preparation 3	1	10	100	100

Preparation 4	1.5	10	150	150
Preparation 5	1.75	10	175	175

Table. 4: Linearity Data Of Magaldrate.

S.No	Concentration (µg/mL)	Area
1	50	424.04
2	75	816.449
3	100	1159.107
4	150	1499.86
5	175	1798.846

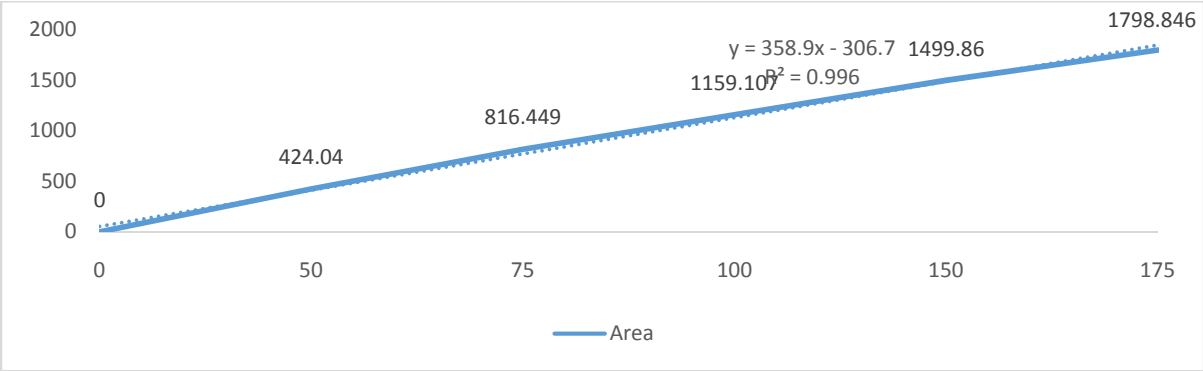


Fig.3:Graph for Linearity data of Magaldrate.

Table. 5: Linearity data of Simethicone.

S.No	Concentration (µg/mL)	Area
1	50	3218.069
2	75	5559.874
3	100	8390.218
4	150	10999.32
5	175	13897.59

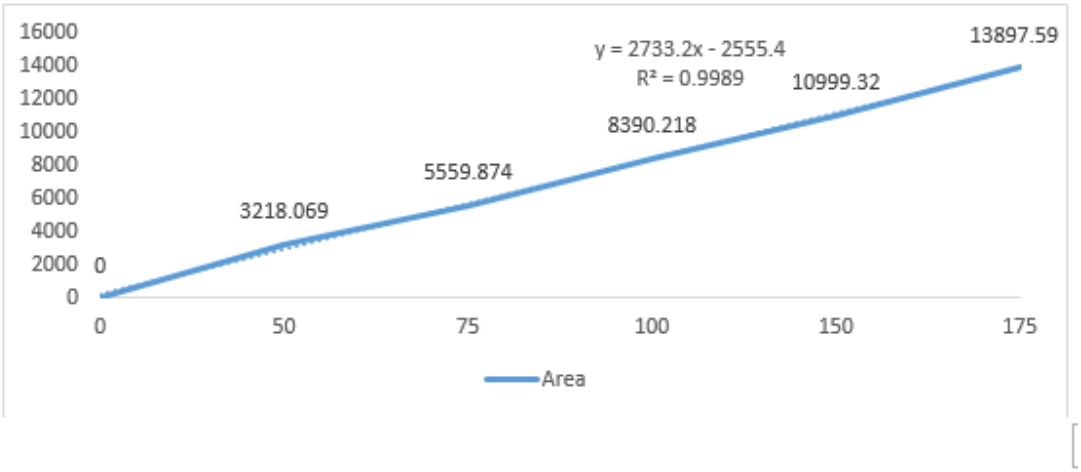


Fig.4: Graph for Linearity data of Simethicone.

Table. 6: Results for Recovery of Magaldrate.

Recovery level	Accuracy Magaldrate Amount Taken(mcg/ml)	Area	Average area	%Recovery	Average % Recovery
	5	913.199			
50	5	901.016	9580.825	98.85	
	5	929.723			
	10	901.016			
100	10	915.556	10285.94	99.80	100.17%
	10	931.069			
	15	929.723			
150	15	1331.21711	704.62	100.86	
	15	1336.835			

Table. 7:Results for Recovery of Simethicone.

Recovery level	Accuracy Simethicone Amount Taken(mcg/ml)	Area	Average area	%Recovery	Average % Recovery
	10	9603.072			
50	10	9605.652	9580.825	99.80	
	10	9533.752			
	20	9605.652			
100	20	10610.71110	285.94	100.50	100.61 %
	20	10641.469			
	30	9533.752			
150	30	12810.23511	704.62	101.55	
	30	12769.881			

Acceptance criteria

The % recovery of Magaldrate and Simethicone should lie between 98% and 102%.

Result

The % mean recovery of Magaldrate and Simethiconewas founded between 100.17% to 100.61%

Robustness

The Robustness of the method was determined. It is obtained by variation in method parameters are summarized below .

Table. 8: Results for Robustness

Parameter	Magaldrate Retention time(min)	Tailing factor	Simethicone Retention time(min)	Tailing factor
		Flow Rate		
0.8 ml/min	2.880	1.054	6.703	1.054
1.2 ml/min	1.987	1.074	4.630	0.932
		Wavelength		
203nm	2.383	1.167	5.530	0.907
207nm	2.377	1.100	5.517	1.021

Ruggedness

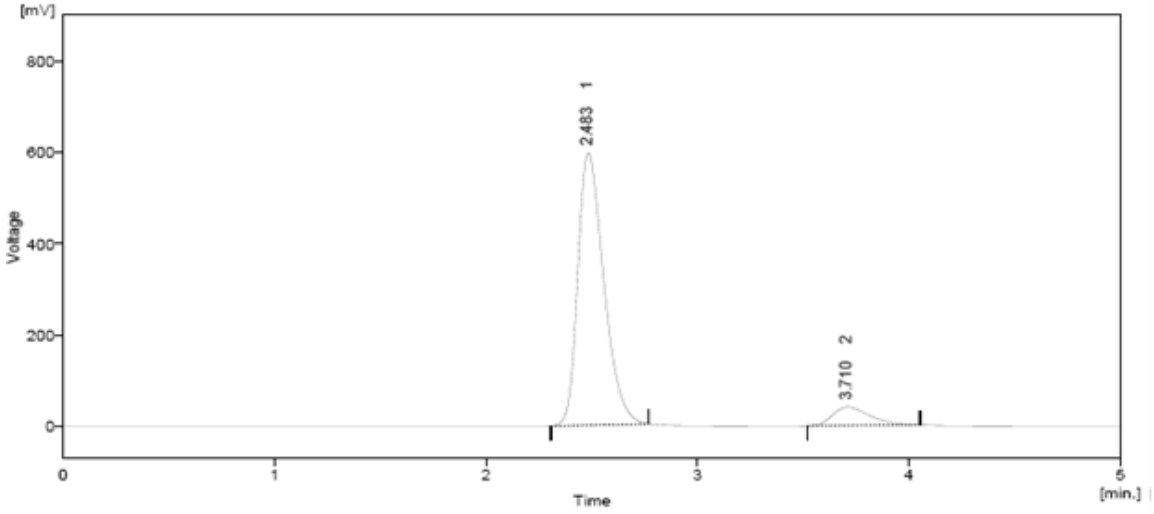
The ruggedness of the method was studied by performing the Assay by two different analysts

Table. 9:Results for Ruggedness

Magaldrate	%Assay	Simethicone	%Assay
Analyst 01	100.5	**Analyst 01**	98.9
Anaylst 02	99.5	**Anaylst 02**	100.6
% RSD	0.45	**% RSD**	1.14

Observation

From the observation the %RSD between two analysts Assay values not greater than 2.0%, hence the method was rugged.



	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	2.483	5098.305	597.085	91.1	93.7	0.13
2	3.710	498.533	40.440	8.9	6.3	0.19
	Total	5596.838	637.525	100.0	100.0	

Column Performance Table

	Reten. Time	W05 [min]	Asymmetry [-]	Capacity [-]	Efficiency [th.pl]	Eff/l [t.p./m]	Resolution [-]
1	2.483	0.133	1.514	0.00	2922	38435	-
2	3.710	0.193	1.621	0.00	2040	40801	4.419

Fig.5: Standard Chromatogram

	Magaldrate		Simethicone	
	Standard Area	**Sample Area**	**Standard Area**	**Sample Area**
Injection-1	9610.218	9618.037	929.107	933.278
Injection-2	9596.321	9610.218	898.86	902.356
Injection-3	9610.218	9545.801	909.64	928.769
Injection-4	9596.321	9394.586	898.86	934.043
Injection-5	9578.389	9612.063	891.613	918.958

Average Area	9598.293	9556.141	578.6002	923.4808
Assay(%purity)	99.5608344		101.972668	

CONCLUSION

From the above it can be concluded that all validation parameters such as precision, accuracy, linearity and Ruggedness met the predetermined acceptance criteria as mentioned in ICH guidelines. The developed RP-HPLC method is simple, rapid, accurate, and precise and can be applied for routine analysis of Magaldrate and Simethicone in bulk and its dosage forms.

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