IJPSR (2021), Volume 12, Issue 2 (Research Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 11 February 2020; received in revised form, 12 May 2020; accepted, 25 May 2020; published 01 February 2021

METHOD DEVELOPMENT AND FORMULATING REBAMIPIDE SUSTAINED RELEASE TABLETS AND ITS EVALUATION

Praveen Kumar [*1], Meenu Chaudhary [2] and Ashutosh Badola [2]

Quantum School of Health Sciences [1], Quantum University, Mandawar, Roorkee - Dehradun Highway (NH 73), Roorkee - 247167, Uttarakhand, India.
School of Pharmaceutical Sciences [2], Shri Guru Ram Rai University, Patel Nagar, Dehradun- 248001, Uttarakhand, India.

Keywords:

Accuracy, Repeatability, Specificity, Precision, Sustained, Rebamipide

Correspondence to Author:
Dr. Praveen Kumar

Associate Professor,
Quantum School of Health Sciences,
Quantum University, Mandawar,
Roorkee - Dehradun Highway (NH 73), Roorkee - 247167, Uttarakhand, India.

E-mail: pkqa1981@gmail.com

ABSTRACT: Last few eras, the remarkable advancement in the drug delivery system has been done; the oral route remains the important and picks up the safest route of drug delivery. Regardless of outstanding advancements in the oral route medication, the current study focused on the formulation of rebamipide SR tablets by studying several blends and their characteristics, including drug-excipients compatibility studies. Ultimately, it was concluded that it is safe to use PEO N12K, Camphor (milled), and MCC in the formulation of the Rebamipide Sustained release tablet. Thus, rebamipide Sustained-release tablets are successfully prepared by using conventional wet granulation technique requires making a matrix type tablet and displaying drug-release through diffusion mechanism. This formulation will assuredly improve patient adherence, improve bioavailability, low side-effects, and sustained clinical activity over the required duration of time (24 h) after single-dose administration. For the determination of the drug content in formulation, a simple, rapid, accurate, robust, and specific UV-Spectroscopy method was developed for the assay of the rebamipide sustained release tablet. The detection was carried out at 325 nm. The linear concentration of standard solutions was approximately 5-60 µg/ml with a linear correlation coefficient of 0.998. The mean recoveries were 99.25%, substantiated the method was accurate. The method was validated concerning linearity, robustness, precision, accuracy, specificity & stability as per ICH guidelines. The proposed research could be successfully applied for the formulation of sustained-release tablets and the determination of rebamipide in SR tablets.

INTRODUCTION: Rebamipide {2-(4-chlorobenzolylamino)- 3- [2(1H)- quinolinon- 4-yl] propionic acid} which is used to treat gastric and gastric mucosal lesions in acute gastritis and acute exacerbation of chronic gastritis [1, 2].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.12(2).1044-52

This article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.12(2).1044-52

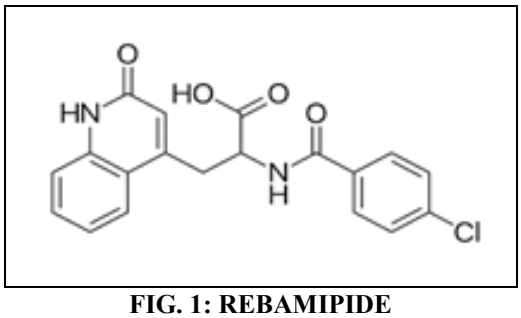

FIG. 1: REBAMIPIDE

Rebamipide makes cyclooxygenase 2 (COX2) synthesis increased mucous secretion [3] enhanced

generations of endogenous prostaglandins [4] suppression of neutrophil function [5] and reserve of inflammatory cytokines [6]. In addition, rebamipide scavenges oxygen-derived free radicals that potentially cause mucosal injury and stimulates prostaglandin EP4 receptor gene expression followed by mucous secretion, thereby enhancing the gastric mucosal defense. The inhibition of immuno-inflammatory replies by Rebamipide in *H. pylori*-infected patients may prevent the development of gastritis, peptic ulcer disease, its repetition, and possibly gastric cancer.

Because of its low solubility and low penetrability, the bioavailability of rebamipide is under 10% in humans; thus, rebamipide is classified into biopharmaceutics classification system IV (BCSIV) [7]. Rebamipide was nearly dissolvable not only in polar but also in non-polar solvents. Shi YJ [8] prepared rebamipide nanosuspensions and improved its oral bioavailability. Nanosuspensions, also called nanocrystals, was regarded as an alternative and promising approach to settle these problems. It is a type of submicron colloidal dispersion system, wherein drug particles are distributed in water with a surfactant or polymer as a stabilizer through self-assembly or broken preparation technology [9, 10].

As a potential technique, nanosuspension has been applied more and more widely to increase the solubility of poorly soluble drugs lately. The solubility was improved by reducing the drug particle size into the nano (sub-micron) range in the usage of nanocrystal technique. In this way, saturation solubility (Cs) was increased, the dissolution rate (dc/dt) and bioavailability (F%) related to the formulation of poorly soluble drugs could be enhanced. At present, both top-down and bottom-up methods are widely used in the field of research in the new dosage form. The top-down wet milling technique can provide highly nanocrystalline with improved physical stability compared with the bottom-up micro-fluidic precipitation method [11-13].

Some methods have been reported for the determination of rebamipide from tablets and human plasma. The method was tedious and time-consuming as it requires a two-step sample preparation procedure while the other method reported based on UV [14], HPLC [15-18], and LC/MS-MS [19]. Which is a modification of the first method and employed a six-port switching valve, a precolumn, and was complex to use. Hence, an attempt precolumn and was complex to use. Hence, an attempt to a rapid, sensitive, accurate and validated UV-spectroscopy method develops for the estimation of rebamipide from SR tablets and applied to pharmaceutical formulations study.

In this study, we adopt a conventional wet granulation method to prepare rebamipide SR tablets. The goal line of this seek was to develop a formulation of rebamipide SR tablets for oral administration and to explore the comparative bioavailability *in-vitro* release. A validated analytical method was developed for the determination of rebamipide in SR tablets.

MATERIALS AND METHODS:

Material: Rebamipide donated by Chongqing Fuan Pharmaceutical (Group) Co., Ltd. Microcrystalline cellulose Magnesium stearate, HPMC, PVP k30, glucose, maltose, lactose, sucrose and mannitol were supplied by Anhui Shahe Pharmaceutic Adjuvant Co. Ltd. All the other chemicals were of analytical grade.

Instrumentation: The Agilent Cary 60 UV-Spectrophotometer of Agilent and Ultrasound bath of PCI make were used in the experiment.

Wet Granulation: The rebamipide SR tablets were prepared by a conventional wet granulation method. Camphor was used as a pore-forming agent. The milled camphor was sieved through a 45-mesh standard sieve rebamipide was mixed with MCC, and kneaded with the addition of a binder solution (5% PVP K30 in 70% EtOH, w/w). The kneaded mixture was passed through a sieve (#30,) and dried in a convection oven at 50 °C for 1 h. The dried granules were sieved (#25) and then homogeneously blended with other excipients. The mixture was lubricated with magnesium stearate and compressed tablets. The tablets were put into a vacuum oven to prepare porous matrices by the sublimation of camphor.

Pre-Compression Study and Evaluation of Rebamipide SR tablets:

Bulk Density: Bulk density is the ratio of the mass by the volume of an untapped powder sample. The

bulk density is measured in g/ml. The bulk density depends on both the density of the powder particles and on the arrangement of the powder particles. The bulk density influence preparation, storage of the sample. The mathematical representation is given below.

Bulk density = Weight of the drug / Bulk volume

TABLE 1: FORMULATION TABLE OF REBAMIPIDE SR TABLET

Ingredients	F 1	F 2	F 3	F 4	F 5	F 6
Rebamipide[a]	300	300	300	300	300	300
MCC[a]	300	300	300	300	300	300
PVP K30a	10	10	10	10	10	10
PEO N12K	150	150	200	150	175	200
Camphor (milled)	150	180	150	180	165	150
MCC	80	50	30	0	65	55
Mg. stearate	10	10	10	10	10	10

Tapped Density: In tapped density, the bulk powder was mechanically tapped in a graduated cylinder until a change in the volume was observed. Here the tapped density is calculated as mass divided by the final volume of the powder.

Tapped density = Weight of the granules / Tapped volume

Angle of Repose: It gives an idea of the flowability of a powder or a bulk solid. There is some factor which responsible for the flowability of powders such as particle size, size distribution, shape, surface area, *etc*. Flowability of the powder depending on the different environments and can be changed easily. The angle of repose was calculated by the following formula.

$$\theta = \tan^{-1} h/r$$

Where, θ = angle of repose, h = height of the formed cone. r = radius of the circular base on the formed cone.

Carr's Index: It is one of the most important parameters to characterize the nature of powders and granules.

Carr's index (%) = Tapped density - Bulk density / Tapped density × 100

Hausner's ratio: It is an important character to determine the flow property of powder and granules. This can be calculated by the following formula

Hausner's ratio = Tapped density / Bulk density

Values less than 1.25 indicate good flow, and greater than 1.25 indicates poor flow.

Friability: Thermionic friabilator was used to determine the friability of the tablets. It is expressed in percentage (%). Initially, ten tablets were weighed and transferred into the friabilator. The total weight of tablets was measured after removing dust on the surface. After performing the friability test for 4 min (25 rpm), dust on the surface of the tablets was carefully removed by blowing air over them. The weight of all tablets was accurately measured, and the reduced percentage of weight of all tablets was calculated, and the result was satisfactory within limits.

% loss = Initial wt. of tablets - Final wt. of tablets × 100 / Initial wt. of tablets

Hardness: Hardness is defined as the force required to break a tablet in a diametric compression test. The devices operating in this manner are the Monsanto tester, the Strong- cobb tester, the Pfizer tester, the Erweka tester, and the Schleuniger tester. Monsanto tester was used to measure the hardness of ten tablets. Mean, and standard deviation was computed and reported. It is expressed in kg/cm^2.

Weight Variation: Twenty tablets were selected randomly from each formulation. Individually weighed tablets and then collectively, the average weight of the tablets was calculated, and then weight variation was calculated.

Thickness: The thickness and diameter of the prepared tablets were evaluated with the help of Vernier calipers and screw gauge.

Drug Content Estimation: Taken the twenty tablets from each formulation were powdered. Taken the powder equivalent to 300 mg of rebamipide was weighed and dissolved in 5ml of water and 60ml of methanol in 100 ml standard

flask Shake for 30 min and then make up the volume with 0.1N HCl. Then taken 5ml of this solution in 50 ml standard flask makeup with 0.1N HCl. Then these samples were analyzed spectrophotometrically at 325 nm.

***In-vitro* Drug Release:** The USP type II dissolution apparatus was used to find out the % of drug release at a regular interval of time. The dissolution medium consists of 900 ml of 0.1N HCL. The temperature was maintained at 37 ± 0.5 °C, at a revolution per minute 100 rpm. Dissolution was carried out, and a regular interval of time 5 ml of sample is pipetted and the same amount of fresh medium replaced in the basket. The collected samples were analyzed under a UV spectrophotometer at 395 nm with suitable dilution. The 0.1N hydrochloric acid was chosen as a blank for the detection of absorbance of the sample and test solution. Pharmacokinetic modelings of drug dissolution profile in order to examine the release mechanism of the drug from the tablets, the *in-vitro* drug release data of rebamipide was carried out for all the formulations with the following release models mentioned below.

- **Zero-order:** Mt = Mo ± Kot
- **First-order:** ln Mt = ln Mo ± K1t
- **Higuchi model:** Mt = KHvt
- **Korsmeyer-Peppas model:** Mt/Mo = Kktn

Where, Mt is the amount of drug dissolved at time t, Mo the initial amount of drug, K1 is the first-order release constant, K0 the zero-order release constant, KH the Higuchi rate constant, Kk the Korsmeyer-Peppas model release constant, and n is the diffusional release exponent indicative of the operating release mechanism. The correlation coefficient (R^2) value was used as an indicator of the best fitting for each of the models considered.

Validated Analytical Method Development for Estimation of Rebamipide According to ICH Guidelines: [20]

Preparation of Standard Stock Solution: Stock solutions of rebamipide was prepared by transferring 50 mg of the drug in 50 ml volumetric flask and dissolved in 30 ml of ethanol and the volume was made up to the mark with ethanol. 5 ml of this solution was transferred to an additional 50 ml volumetric flask and further diluted up to 50 ml mark with ethanol. This standard solution contained 100 µg of drug per ml.

Selection of Wavelength Maxima (λ_{max}): Pipette out 1 ml of working standard solution and transfer into 10 ml volumetric flask and the volume was made up to the mark with solvent to get the concentration 10 µg/ml. The resulted 10 µg/ml solution was scanned in UV-Spectrophotometer between 200-400 nm using ethanol as blank. The wavelength maxima were established at 325 nm.

Preparation of Calibration Curve: Pipette out 0.5, 1, 2, 3, 4, 5 and 6 ml working standard solution and transfer into seven separate 10 ml volumetric flasks and made the volume all of them to 10 ml with ethanol to get the concentrations 5, 10, 20, 30, 40, 50 and 60 µg/ml respectively. The absorbance of the resultant solution was measured at 325 nm using ethanol as blank. A graph was plotted between the concentrations and their respective absorbance and find out the linearity and range with a correlation coefficient.

Repeatability: Pipette out 1, 2, 3 ml standard solution and transfer into a series of nine, 10 ml volumetric flasks. Dilute it to 10 ml with ethanol to get 10, 20, 30 µg/ml solutions, respectively. The absorbance of the resultant solutions was measured at 325 nm using ethanol as blank.

Intra-Day Precision: Pipette out 1, 2, and 3 ml working solution and transfer into separate 10 ml volumetric flasks and made up the volume to 10 ml with ethanol to get the concentrations 10, 20, and 30µg/ml respectively. The absorbance of the resultant solutions was measured at 325 nm using ethanol as blank. Such three revisions were performed within a day at 3 h intervals.

Inter-Day Precision: Pipette out 1, 2, and 3ml working solution and transfer into separate 10 ml volumetric flasks. Dilute all of them to 10 ml with ethanol to get a solution of concentrations 10, 20, and 30µg/ml, respectively. The absorbance of the resultant solutions was measured at 325 nm using ethanol as blank. Such three studies were performed for day one, day two, day three intervals.

Accuracy: Pipette out 1.5ml standard solution and transfer into 10 ml volumetric flasks. Nine such transfers were made. Spike three of the volumetric flask with the solutions with 1.2 ml of working solution (prepared from formulation) and dilute each to 10 ml with ethanol to get 12 µg/ml solutions. Spike another three of the solutions with 1.5 ml of working solution and dilute each to 10 ml with ethanol to get 15 µg/ml solutions. Spike the last three of the solutions with 1.8 ml of working solution and dilute each to 10 ml with ethanol to get 18 µg/ml solutions. The absorbance of the resultant solutions was measured at 325 nm using ethanol as blank.

Specificity: Specificity study was carried out by observing any interference in absorbance of drug in the presence of common excipients like starch, talc, lactose, magnesium stearate, *etc*. The absorbance of 10 µg/ml drug solution with and without excipients was measured at 325 nm using ethanol as blank.

Estimation of Rebamipide in SR Tablets Dosage Form: Weigh 20 tablets and calculates the average weight of the tablets. Powered the tablets and weigh accurately a quantity of powdered containing about 50 mg of rebamipide and transfer it into 50 ml volumetric flask and add 30 ml ethanol, sonication for 10 minutes and made up the volume to 50 ml with solvent then mix and filter that solution. Taken 5 ml of the filtrate and made up the volume to 50 ml with ethanol. Further, dilute 1 ml of the resulting solution to 10 ml with ethanol in three volumetric flasks and made up the volume to the mark. Measure the absorbance of these resulting solutions at 325 nm.

RESULTS AND DISCUSSION:

Pre-formulation Study for all Formulations: Bulk density and tapped density mainly depends on the nature of the compound and its size. These properties of a compound may vary due to the crystallization, milling, or formulation. It also provides true acquaintance of the size of the final dosage form. The density of the solid also affects its compression and flow assets after final production. The Pre compression results of rebamipide have been reported in **Table 2**. The bulk density of the formulations was found to be 0.335 to 0.412 gm/ml, tapped density shows the array between 0.409 to 0.476 gm/ml, angle of repose between the range of 25.68 to 28.98, and Hauser's ratio value lies between 1.15 to 1.24. Obtained results were within limits and observed excellent flow properties.

TABLE 2: PRE FORMULATION STUDY FOR REBAMIPIDE FORMULATION (F_1-F_6)

Formulation	Bulk density	Tapped density	Carr's Index	Hausner's Ratio	Angle of Repose
F1	0.372	0.455	1.23	1.22	27.89
F2	0.382	0.462	1.21	1.20	28.35
F3	0.412	0.478	1.16	1.16	28.98
F4	0.355	0.409	1.14	1.15	28.97
F5	0.382	0.476	1.22	1.24	25.68
F6	0.396	0.473	1.10	1.19	26.42

Post-compression Study of Rebamipide SR Tablets (F_1-F_6): Rebamipide SR tablets (Formulation F1-F6) were evaluated for their physicochemical properties that play a vital role in the drug release pattern. A comparison of the physicochemical properties of all the formulations is listed in **Table 3**. The weight variation was found to be within the limit of ± 5%. The average weight for all formulations was found to be in the range of 795 to 803 mg. The measurement of thickness has been carried out by Vernier caliper. Thickness is an important parameter that helps in the ease of swallowing of tablets. Obtained results concluded that uniform thickness has been observed for all formulations and found within the range of 3.83 to 3.96 mm. The formulated tablets passed through the hardness and friability tests as per the standard limits, the hardness ranging from 5.80 to 6.6.2, and the percentage of friability obtained below 1%. The friability and hardness of the tablet are directly implicated to the strength of the tablet and an important factor in controlling the damage during the transportation and handling of the tablet. Similarly, drug content % for all the formulation was within the range between 99.65 to 100.2%. Obtained results confirm that evaluation parameters are within the limit as per Indian Pharmacopeia for all the formulations.

TABLE 3: POST-COMPRESSION STUDY OF REBAMIPIDE SR TABLETS (F_1-F_6)

Formulation	Hardness (Kg/cm^2)	Friability (%)	Thickness (mm)	Weight Variation (%)	Drug Content (%)
F1	5.8	0.370	3.86	803	99.45
F2	6.0	0.190	3.96	799	99.56
F3	5.9	0.356	3.94	800	99.63
F4	6.2	0.415	3.92	801	98.89
F5	5.7	0.413	3.89	795	99.65
F6	6.1	0.449	3.83	798	100.2

***In-vitro* Drug Release:** The dissolution was carried out triplicate by utilizing the diffusion medium 0.1 N HCl. The percentage of drug release for all rebamipide formulations F1 to F6 ranged from 75% to 99.21% at the end of 12 h. Maximum drug release in a controlled manner was observed in the formulation F3 after 12 h. The reason for maximum release may be due to the combination of different polymers at different concentration and the viscosity nature of polymers. Drug release % was calculated for rebamipide SR tablet formulations F1 to F6, shown in **Table 4.**

TABLE 4: *IN-VITRO* DISSOLUTION PROFILE FOR REBAMIPIDE SR TABLETS (F_1-F_6)

Time (h)	F1	F2	F3	F4	F5	F6
1	15.74	14.96	11.68	13.00	12.57	14.46
2	20.46	22.69	18.89	21.70	20.99	19.06
4	36.35	32.61	28.7	22.01	29.83	25.38
6	54.83	49.20	41.97	45.5	48.35	32.55
8	75.21	70.56	64.22	66.6	56.91	49.37
10	87.32	92.86	80.88	81.12	74.25	60.62
12	89.66	--	99.21	86.60	75.90	78.96

Analytical Method Development: The UV-Spectroscopy method was developed and optimized after a series of trials in terms of detection of wavelength maxima of rebamipide by the overlay UV spectrum is represented in **Fig. 2**. Rebamipide showed absorption maxima at 395 nm.

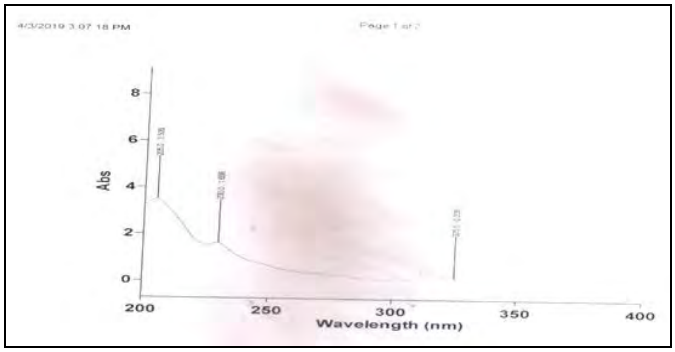

FIG. 2: WAVELENGTH MAXIMA OF REBAMIPIDE IN ETHANOL

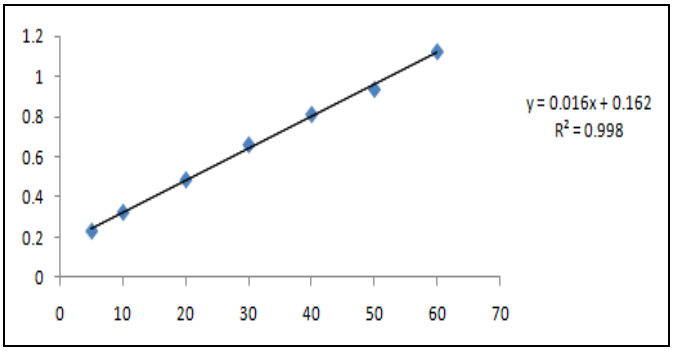

FIG. 3: CALIBRATION CURVE OF REBAMIPIDE IN ETHANOL

Method Validation: The calibration equation for rebamipide was obtained y = 0.016x + 0.1621 and linear within the concentration range of 5 - 60 µg/ml with correlation coefficient values 0.998. The calibration curves, linearity, $E^{1\%}{}_1$cm, absorptivity (l gm^{-1} cm^{-1}) and molar absorptivity (l mol^{-1} cm-^{1}) of rebamipide given in **Fig. 3** and **Table 5**.

TABLE 5: LINEARITY, $E^{1\%}{}_1$ABSORPTIVITY (L gm^{-1} cm^{-1}), MOLAR ABSORPTIVITY (L mol^{-1} cm^{-1})

S. no.	Concentration (µg/ml)	Absorbance at 325nm	$E^{1\%}{}_{1CM}$	Absorptivity	Molar Absorptivity
1	5	0.2290	458	45.8	16981.9988
2	10	0.3229	322.9	32.29	11972.6799
3	20	0.4851	242.55	24.255	8986.1379
4	30	0.6603	220.1	22.01	8160.999
5	40	0.8117	202.925	20.2925	7524.174905
6	50	0.9364	187.28	18.728	6944.0802
7	60	1.1248	187.46666	18.746	6950.7543
		Mean	260.1745	26.01745	29947820.001

Precision: The results of three replicate of mixed standard solutions showed very low %RSD. In the repeatability test, the % RSDs for six determinations were found to be 0.57% for rebamipide and results are reported in **Table 6**. The inter-day and intraday precisions results for assay were found to be very precise with low %RSD for both components of all three brands, and results were summarised in **Table 7** and **8**.

TABLE 6: STUDY OF REPEATABILITY

Concentration (µg/ml)	Absorbance	Observed Concentration (µg/ml)	Mean Concentration (µg/ml)	SD	RSD
10	0.3221	9.9	0.3203	0.00156	0.48768
	0.3193				
	0.3195				
20	0.4920	20.1	0.4934	0.00257	0.52078
	0.4919				
	0.4964				
30	0.6382	29.8	0.6383	0.00036	0.5649
	0.6380				
	0.6387				

TABLE 7: STUDY OF INTRA DAY PRECISION

Conc.(µg/ml)	Absorbance			Observe absorbance			Mean	SD	RSD
	0 h	3 h	6 h	0 h	3 h	6 h			
	0.3315	0.3367	0.3390	9.8	10	10.3			
10	0.3408	0.3379	0.3392	10	10	10.3	0.3370	0.00363	1.0849
	0.3263	0.3431	0.3389	10	10	10.3			
	0.4920	0.4991	0.4965	19.9	20.1	20			
20	0.4991	0.4964	0.4920	19.9	20.1	20	0.4934	0.00257	0.52078
	0.4964	0.4920	0.4991	20	20	20			
	0.6448	0.6449	0.6380	29.9	30.2	29.8			
30	0.6442	0.6449	0.6382	30.2	30.2	29.8	0.6426	0.00033	0.05045
	0.6441	0.6454	0.6386	30.2	30.2	29.8			
								Mean	0.5520

TABLE 8: STUDY OF INTER DAY PRECISION

Conc.(µg/ml)	Absorbance			Observe absorbance			Mean	SD	RSD
	0 h	24 h	48 h	0 h	24 h	48 h			
	0.3390	0.3392	0.3390						
10	0.3392	0.3389	0.3389	9.9	10	9.8	0.3390	0.00015	0.04505
	0.3389	0.3390	0.3392						
	0.5013	0.5009	0.5010						
20	0.5008	0.5011	0.5013	19.9	20	19.8	0.5010	0.00025	0.05022
	0.5010	0.5012	05011						
	0.6447	0.6445	0.6446						
30	0.6442	0.6449	0.6448	29.9	30	30.2	0.6446	0.00036	0.05593
	0.6449	0.6447	0.6449						
								Mean	0.0504

Accuracy: The amount of drug recovered was calculated in each case. The percentage of recovery was calculated by using the following formula, % accuracy = (Amount of drug recovered in mg/ Amount of drug added) in mg ×100, and the result for all the nine determinations is presented in **Table 9** for rebamipide.

The method was proved to be very accurate as the recovery for rebamipide was 99.25% and 100.62% for all the three levels *i.e.,* 90%, 100%, and 120%.

Specificity: Specificity study was carried out by observing any interference in absorbance of the drug in the presence of common excipients like starch, talc, lactose, magnesium stearate, *etc*. The absorbance of 10 µg/ml drug solution with and without excipients, the results obtained were within limits and summarized in **Table 10**.

Assay of Rebamipide in SR Tablets: The method was found to be very accurate, and the result obtained was summarized in **Table 11**.

TABLE 9: STUDY OF ACCURACY

Recovery at	Nominal Conc. (µg/ml)	Absorbance	Observed Conc. (µg/ml).	% Recovery
90%	27=15+12	0.5709	26.8	99.25%
90%	27=15+12	0.5706	26.6	98.51%
90%	27=15+12	0.5702	26.9	100.62%
100%	30=15+15	0.6403	29.9	99.66%
100%	30=15+15	0.6391	29.8	99.33%
100%	30=15+15	0.6385	29.8	99.33%
120%	33=15+18	0.6923	33.2	100.60%
120%	33=15+18	0.6929	33.2	100.60%
120%	33=15+18	0.6918	33.2	100.60%
			Mean	99.72(±)0.70

TABLE 10: STUDY OF SPECIFICITY

Nominal Conc. (µg/ml)	Without excipient		With excipients		% Interference
	Absorbance	Observed conc.	Absorbance	Observed conc.	
10	0.3272	10.3	0.3365	10.4	1.0097
10	0.3203	9.9	0.3372	10.4	1.05
10	0.3241	10.1	0.3135	10	1.01
10	0.3252	10.2	0.3298	10.3	1.0098
10	0.3250	10.2	0.3364	10.4	1.019
10	0.3247	10.2	0.3392	10.5	0.971
				Mean	0.8659

TABLE 11: % ASSAY OF REBAMIPIDE IN REBAMIPIDE SR TABLETS

S. no.	Absorbance	Concentration (µg/ml)	Dilution Factor	Weight Taken (mg)	Average Weight (mg)	Label Claim (mg)	% Assay
1	0.3154	9.8	5000	122.75	245.5	100	98%
2	0.3185	9.9	5000	122.75	245.5	100	99%
3	0.3195	9.9	5000	122.75	245.5	100	99%
4	0.3241	10.1	5000	122.75	245.5	100	101
						Mean	99.25%

CONCLUSION: The current research focused on the development of rebamipide SR tablets incorporating different types of the polymer at different composition ratios. Polymers are hydrophilic and hydrophobic in nature, and containing gelling property is useful for control the release rate of drug content from the formulation. Pre and post-compression evaluation parameter values show within the limit of IP. The *in-vitro* dissolution study was conducted for all the formulations (F1-F7) and found that as an individual polymer has shown complete drug release of rebamipide, whereas PEON 12 K shows incomplete release. In formulation F3, which contains PVP K30: PEO N 12 K: Camphor in the ratio of 1:20:15 respectively, has shown better control in the release rate of the drug in SR tablet almost 100% at 12 h. A combination of the hydrophobic and hydrophilic polymer could be a good carrier for controlling the release rate of the drug in SR tablet.

The proposed method is supported by full validation parameters and proved to be very specific for all the formulations of rebamipide. The accuracy is established from precise assay results (low % RSD). The method offers simplicity in terms of short analysis time, easy sample preparation technique. The method has produced good specificity and shown accurate results for finished product formulations without any interference from the excipients. So, these advantages make this method reliable for the intended purpose.

ACKNOWLEDGEMENT: The authors thank the management of Quantum University and Shri Guru Ram Rai University for their continuous support and encouragement. Thanks are also owed to the Quantum School of Pharmaceutical Sciences for instrumentation facilities to carry out the work.

CONFLICTS OF INTEREST: The authors have declared no conflicts of interest.

REFERENCES:

1. Huang BB, Li GF and Luo JH: Permeability's of rebamipide *via* rat intestinal membranes and its colon

specific delivery using chitosan capsule as a carrier. World J Gastroenterol 2008; 14: 4928-37.
2. Arakawa T, Higuchi K and Fujiwara Y: 15th anniversary of rebamipide: looking ahead to the new mechanisms and new applications. Dig Dis Sci 2015; 50: S3-11.
3. Guo Y, Yongjun, Wang and Xu L: Enhanced bioavailability of rebamipide nanocrystal tablets: Formulation and *in-vitro*/*in-vivo* evaluation. Asian J of Pharma Sci 2015; 10(3): 223-29.
4. Abrahamsson B, Alpsten M and Hugosson M: Absorption, gastrointestinal tran-sit, and tablet erosion of felodipine extended-release (ER) tablets. Pharm Res 1993; 10(5): 709-14.
5. O'Reilly S, Wilson C and Hardy J: The influence of food on the gastric emptying of multiparticulate dosage forms. Int J Pharm 2017; 34: 213-16.
6. Genta RM: The role of rebamipide in the management of inflammatory disease of the gastrointestinal tract. Aliment Pharmacol Ther 2018; 18(1): 8-13.
7. Dolas RT, Sharma S and Sharma M: Formulation and evaluation of gastroretentive floating tablets of rebamipide. Int J of Pharmacy and Analytical Res 2018; 7(3): 446-55.
8. Shi YJ, Zou MJ and An Y: A potent preparation method combining neutralization with microfluidization for rebamipide nanosuspensions and its *in-vivo* valuation. Drug Dev Ind Pharm 2012: 1-9.
9. Kim KT, Lee JY, Park JH, Cho HJ, Yoon IS, Kim DD: Capmul MCM/Solutol HS15-based microemulsion for enhanced oral bioavailability of rebamipide. J Nanosci Nanotechnol 2017; 17: 2340-44.
10. Tuomela A, Liu P and Puranen J: Brinzolamide nanocrystal formulations for ophthalmic delivery: reduction of elevated intraocular pressure *in-vivo*. Int J Pharm 2014; 467: 34-41.
11. Ali HS, York P and Ali AM: Hydrocortisone nano-suspensions for ophthalmic delivery: a comparative study between microfluidic nanoprecipitation and wet milling. J Control Release 2011; 149: 175-81.
12. Pradhan R, Tran TH, Choi JY, Choi IS, Choi HG and Yong CS: Development of a rebamipide solid dispersion system with improved dissolution and oral bioavailability. Arch Pharm Res 2015; 38: 522-33.
13. Calcinari R: The zeta potential and its value in pharmaceutical technology. Farmaco Prat 1970; 25: 24-38.
14. Srivastava PK and Roy A: Development and Validation of a New UV Method for the Analysis of Rebamipide. International Journal of PharmTech Research 2011; 3(3): 1270-74.
15. Patel P, Poshiya P and Chauhan G: Development and validation of high performance thin layer chromatographic method for determination of Rebamipide from its tablet dosage form. International Journal of Pharmacy and Pharmaceutical Sciences 2014; 6(5): 606-10.
16. Jeoung MK, Kim CS, Kim NH, Hong JT, Chung YB, Park Y, Kim KS and Moon DC: Determination of Rebamipide in human plasma by HPLC. J of Liquid Chromat & Related Technologies 2004; 27(12): 1925-35.
17. Manglani UR, Khan IJ, Soni K, Loya P and Saraf MN: Development and validation of HPLC-UV method for the estimation of Rebamipide in human plasma. Indian J Pharm Sci 2006; 68(4): 475-78.
18. Cooper DL and Harirforoosh S: A simple high performance liquid chromatography method for determination of Rebamipidein rat urine. Methods X 2014; 1: 49-55.
19. Liu J, Shen-Tu J, Wu L, Dou J, Xu Q, Zhou H, Wu G and Hu X: Development of a simple LC-MS/MS method for determination of Rebamipidein human plasma and its application to a bioequivalence study. Die Pharmazie-An Int J of Pharma Sci 2012; 67(11): 906-11.
20. International Conference on Harmonization (ICH) Validation of Analytical Procedures: Text and Methodology Q2 (R1). Geneva 2005.

How to cite this article:
Kumar P, Chaudhary M and Badola A: Method development and formulating rebamipide sustained release tablets and its evaluation. Int J Pharm Sci & Res 2021; 12(2): 1044-52. doi: 10.13040/IJPSR.0975-8232.12(2).1044-52.