RESEARCH ARTICLE

Solubility Enhancement of Low Water Soluble Drug Using Granulating Agents

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ABSTRACT

Class II drugs are characterized by their poor aqueous solubility and good permeability (As per BCS Classification). Therefore, formulating these types of drugs becomes very tricky and challenging. Incomplete and non-uniform release of these drugs causes less absorbance and poor bioavailability. Hence, there is huge requirement for build up a new strategy for this Class II category drugs for increasing their bioavailability and drug release.

The low aqueous solubilization of API directly affects the drug release as well as its permeability through membrane or bioavailability. Therefore it is required to modify the solubility of these drugs by using suitable components which can enhance their solublization in the biological media. This study covered the solubility enhancing trials done with the active molecule Celecoxib. In this study multiple type of granulating agents were used for formulation of the tablet and their physicochemical characteristics were evaluated.

Keywords: Granulating Agents, Solubility, Bioavailability, Drug Release

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INTRODUCTION

For enhancing the drug solubilization, multiple techniques are available in the pharmaceutical world like micronization of drug, their salt formation, using the suitable surfactant or co-solvent[1]. To get the complete benefit of the drug or desired therapeutic profile, it is required that at the absorption site drug (active moiety) must be released completely from its dosage form. Quality characteristics of any dosage form are defined by its drug release characteristics in the biological fluid or its bioavailability[2-3]. Bioavailability is also known as, "the amount of drug which reaches into the blood plasma through the biological membrane". In other words time duration and quantity of active moiety reaches into the biological fluid circulation from the drug formulation is known as bioavailability[4-5]. Hence, the bioavailability for the injectable dosage forms was observed to be 100%. But the injectable formulations are less acceptable due to multiple reasons like patient unacceptability, painful administration and their less stability during storage. Therefore, from the view of patient, oral route for the administration of dosage form is always most preferred and desirable[6]. However, there are some limitations associated with these types of formulations like the physicochemical properties of the drug, type of dosage form or formulation and the behavior of patient. Quality characters of the finished product are affected by the various formulation and manufacturing process parameters. In the formulation part, characteristics of the active drug molecule like its Particle size, solubility, crystallinity, flowability, compressibility, compatibility with other excipients and its stability in the dosage form. Additionally in the formulation, type and the quantity of excipient also have the impact on the finished dosage form behavior[7]. In the Manufacturing process Type of granulation, quantity and addition time of Granulating agent, Drying time, Water content of dried granules, Lubrication time, Compression force or Tablet strength etc affects the characteristics of the finished dosage form.[8]

MATERIALS AND METHODS

Celecoxib was received as gift sample from M/s Ind-Swift limited and other excipients received from different vendors as gift sample.

Standard Curve

Multiple strength of Celecoxib i.e. 5µg, 10µg, 15µg, 20µg and 25µg per ml were prepared after dilution of the Standard solution of Celecoxib with the required quantity of 0.1N HCl.

Testing vials were scanned against the 0.1N HCl as a blank, in spectroscopy at the λ of 254 nm.

Manufacturing of Tablets

According to Table 1.0 composition, Celecoxib, Pharmatose, and Avicel were combined and passed through mesh number 20. Binder agent was prepared using purified water. This binder solution was used for granulation of dry mix powder. Wet mass was dried at 60°C for 35 minutes. Dried granules were further sized using suitable sieve. Dried granules were lubricated using lubricants and compressed into the tablet form.

Evaluation of Tablets

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Table 1: Formulation composition

Component	E1 (Qty/tab.)	E2 (Qty/tab.)	E3 (Qty/tab.)	E4 (Qty/tab.)	E5 (Qty/tab.)	E6 (Qty/tab.)	E7 (Qty/tab.)
Celecoxib	100.00 mg	100.00 mg	100.00 mg	100.00 mg	100.00 mg	100.00 mg	100.00 mg
Gum Arabic	4.00 mg	0.00	0.00	0.00	0.00	0.00	0.00
Pharma sugar	0.00	4.00 mg	0.00	0.00	0.00	0.00	0.00
Plasdone	0.00	0.00	4.00 mg	0.00	0.00	0.00	0.00
Carbowax	0.00	0.00	0.00	4.00 mg	0.00	0.00	0.00
Metolose	0.00	0.00	0.00	0.00	4.00 mg	0.00	0.00
Starch Paste	0.00	0.00	0.00	0.00	0.00	4.00 mg	0.00
Crayogel	0.00	0.00	0.00	0.00	0.00	0.00	4.00 mg
Avicel	43.00 mg	43.00 mg	43.00 mg	43.00 mg	43.00 mg	43.00 mg	43.00 mg
Talcum	2.00 mg	2.00 mg	2.00 mg	2.00 mg	2.00 mg	2.00 mg	2.00 mg
Compritol	3.00 mg	3.00 mg	3.00 mg	3.00 mg	3.00 mg	3.00 mg	3.00 mg
Pharmatose up to	200.00 mg	200.00 mg	200.00 mg	200.00 mg	200.00 mg	200.00 mg	200.00 mg

Tablets were crushed into the form of fine powder. This powder form was dissolved in the solvent and further diluted with the dissolution media. This solution was analyzed using UV visible spectroscopy at the wavelength of 254 nm. Tablet Hardness, Friability and Disintegration time was analyzed by using respective equipments. Drug dissolution was analyzed using Dissolution test apparatus using 0.1N HCl as dissolution media. Sample collected at different time periods were treated with sufficient dilution media and analyzed using UV-Visible spectroscopy at the wavelength of 254 nm.

RESULTS AND DISCUSSION

Calibration Curve

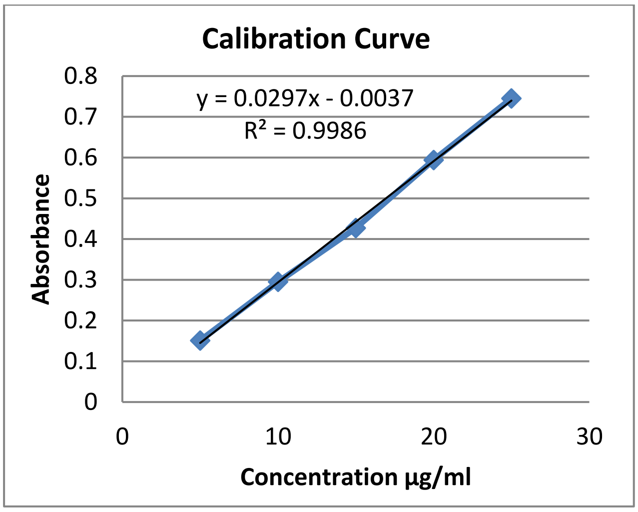

Figure 1: Calibration Curve of Celecoxib

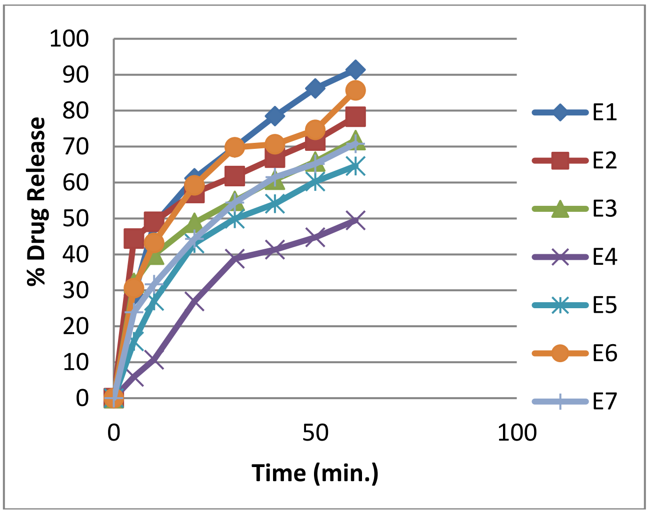

Figure 2: Percentage Drug Release of Tablets

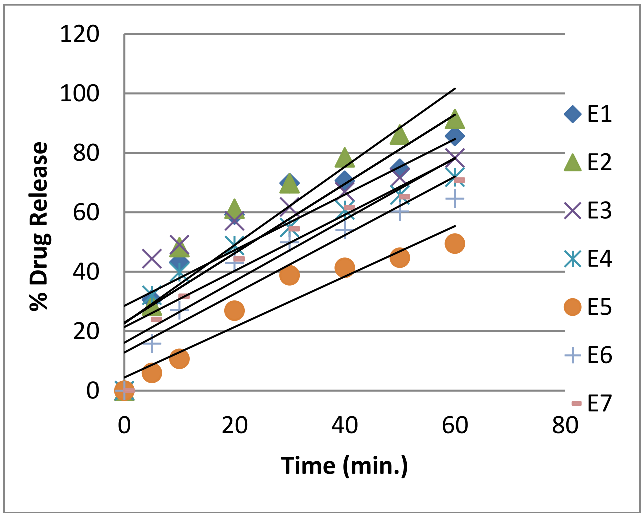

Fig. 3.0: Zero order drug release kinetics

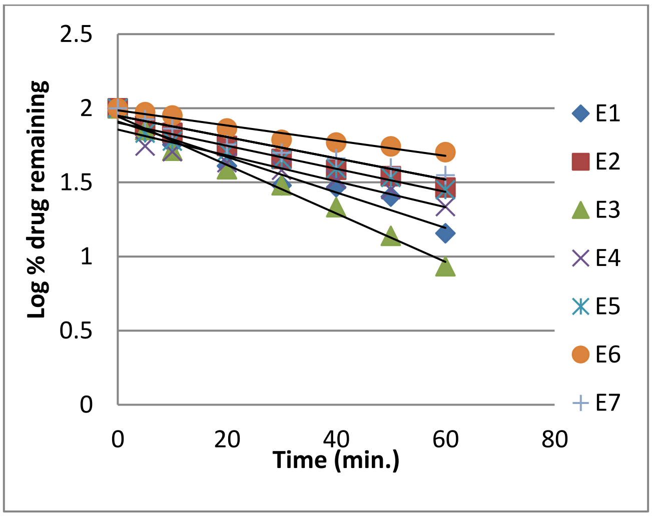

Fig. 4: First order drug release kinetics

Table 2: Calibration curve of Celecoxib

Concentration	Absorbance
5 µg/ml	0.151
10 µg/ml	0.295
15 µg/ml	0.427
20 µg/ml	0.594
25 µg/ml	0.745

The observed results are mentioned in Table 2.0 & Fig. 1.0. As per the results this method follows the Beer's law. Hence this method can be utilized for the *in-vitro* drug dissolution study.

Table 3: Physical Parameters of Tablets

Formulation	Drug Content	Hardness	Friability	DT
E1	100.8	4.0-6.0 Kp	0.45%	2.7 min
E2	100.3	7.0-8.0 Kp	0.76%	0.7 min
E3	100.2	4.3-5.0 Kp	0.53%	2.0 min
E4	99.7	11-12 Kp	0.20%	18.0 min
E5	99.4	11-12 Kp	0.18%	16.0 min
E6	100.1	4.5-5.5 Kp	0.45%	1.1 min
E7	99.6	4.5-5.5 Kp	0.10%	1.0 min

Table 5. Values of (r) according to Zero order and First Order Kinetics

Formulation	Zero Order R^2	First Order R^2
E1	0.853	0.986
E2	0.701	0.885
E3	0.815	0.937
E4	0.927	0.956
E5	0.887	0.957
E6	0.818	0.942
E7	0.882	0.968

Evaluation of Tablets

Physical parameters of the different formulations are as per the Table 3.0. For different formulations observed tablet harness was satisfactory i.e. 4.0 Kp to 12 Kp. Additionally the tablets friability was also within the Pharmacopoeial acceptance criteria. Disintegration time of the all formulations was satisfactory except the formulation E4 & E5. In those formulations DT was observed to be more than 15 min. Assay of the drug for all formulations were also well within the acceptance criteria. Among all formulation drug dissolution profile (Table 4.0; Fig. 2.0) for the formulation E1 was satisfactory. In rest of the formulations incomplete drug release was observed. Release kinetics and their R^2 values are mentioned in Fig. 3 & 4 and Table 5.0. As per the Results Drug release for all formulations are following first order kinetics.

CONCLUSION

Solubility of the drug is characterized by its dissolution behavior in the media. In this study it was observed that the formulation manufactured using the granulation agent Gum Arabic has satisfactory and complete drug release when compared to other drug release. Therefore, it can be concluded that the solubility of the drug increases to a satisfactory level in the presence of Gum Arabic, starch, and pharma sugar as compared to others.

REFERENCES

1. Suttee A, Pavani S. Formulation and Evaluation of Buccoadhesive Tablets of Diltiazem Hydrochloride. International Journal of Drug Delivery Technology. 2022;12(3):981-984.
2. Saffari M, Ebrahimi A, Langrish T. A novel formulation for solubility and content uniformity enhancement of poorly water-soluble drugs using highly-porous mannitol. Eur J Pharm Sci. 2016; 83:52-61.
3. L. Smitha and S. Pavani M. Keerthana. Formulation and evaluation of propranolol hydrochloride oral disintegrating tablets. International journal of pharmaceutical sciences and research 2021; 12(11): 5916-5921.
4. Agrawal R., Mishra PG, Bansal B. Understanding Degradation Pathway of Poorly Stable Diltiazem Hydrochloride and Development of its Stabilized Controlled-release Tablets. International Journal of Drug Delivery Technology. 2022;12(4):1646-1649.
5. Kumar P, Kijjal R. Novel oral sustained release drug technology. A concise review. International Journal of Research and Development Pharmaceutical Sciences.

Table 4: Drug Release of Tablets

Time	% Release (X + SD)						
	E1	E2	E3	E4	E5	E6	E7
5 min	28.65% ± 1.2	44.41% ± 1.30	32.10%± 1.50	5.95%± 0.95	15.81%± 0.95	30.61%± 1.30	23.91%± 1.10
10 min	48.31% ± 1.40	49.10% ± 1.20	39.90%± 1.20	10.71%± 1.10	27.05%± 1.40	43.21%± 1.10	31.70%± 1.20
20 min	61.20% ± 1.50	57.10% ± 1.20	48.81%± 1.10	26.91%± 0.93	43.01%± 1.10	59.21%± 1.40	44.30%± 1.20
30 min	69.78% ± 1.10	61.80% ± 1.40	54.90%± 0.93	38.80%± 1.40	49.91%± 1.30	69.81%± 0.95	54.41%± 1.40
40 min	78.50% ± 0.95	66.90% ± 1.10	60.80%± 1.40	41.32%± 1.10	54.10%± 1.10	70.65%± 0.93	61.51%± 0.95
50 min	86.20% ± 1.60	71.70% ± 0.94	65.85%± 1.20	44.75%± 1.30	60.28%± 0.96	74.65%± 1.30	65.20%± 1.10
60 min	91.40% ± 1.40	78.30% ± 1.30	71.80%± 1.10	49.48%± 1.10	64.61%± 1.10	85.65%± 1.20	70.81%± 1.40

2013; 2: 262-69.

6. Sun W, Ni R, Zhang X, Li LC, Mao S. Spray drying of a poorly water-soluble drug nanosuspension for tablet preparation: formulation and process optimization with bioavailability evaluation. Drug Dev Ind Pharm. 2015; 41(6): 927-33.
7. Murtaza G, Khan S A, Najam-ul-Haq M, Hussain I. Comparative evaluation of various solubility enhancement strategies for furosemide. Pak J Pharm Sci. 2014; 27(4):963-73.
8. Jain SC, Agrawal GP. Indian Drugs. 1981; 19: 108.