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RESEARCH ARTICLE

Improvement of Solubility by Disintegrating Approach of Poorly Soluble Drugs in Capsule Dosage Form

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ABSTRACT

Celecoxib belongs to the category of NSAIDS. This drug is used for treatment of rheumatoid arthritis and acute pain during menstruation. Celecoxib is poorly soluble and the intention of the study is to improve the solubility by disintegration approach. Different mixture of disintigrants are used in the preparation of celecoxib by wet granulation method and supplied in gelatin capsule dosage form. Eight different batches are prepared by using different disintigrants in different quantities along with other excipients and then they are evaluated by different parameters. The study demonstrated that celecoxib capsule prepared with various disintegrants showed significantly higher dissolution in comparison with physical powder mixture having same drug excipients ratio. Different mixture of disintigrants is use in the preparation. Out of the disintegration studied Polyplasdone XL 10 grades were superior than the other disintegrates for the drug studied. The combined effect of Polyplasdone XL 10 and cross Carmellose sodium gives better dissolution than individually. So ultimately combined effect of two disintegrants and low grade povidone K30 will give more than 80% dissolution within 30 min.

KEYWORDS

Celecoxib, Disintegrates, Menstruation, Polyplasdone XL 50, Rheumatoid arthritis

INTRODUCTION

Administration among all the routes that have been explored for the systemic delivery of drugs oral drug delivery has been known for decades as the most widely utilized route of via various pharmaceutical products of different dosage forms. In oral route of administration at that time solubility plays an important role. When solubility of the drug is high absorption of drug is high so that bioavailability of the drug is also increase. When the drug is poorly soluble the bioavailability of the drug is very low and the proper effect does not seen in that case. The drug will dissolve at a slower rate from a non disintegrating tablet due to exposure of limited surface area to the fluid.

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The disintegration test is an official test and hence a batch of tablet must meet the stated requirements of disintegration. Disintegrant is an important excipient of the tablet formulation, are always added to tablet to induce breakup of tablet when it comes in contact with aqueous fluid.

The various disintegrants includes synthetic derivatives such as sodium carboxy methyl cellulose, crosspovidone, sodium starch glycollate, cross carmellose sodium, and natural derivatives such as alginates, cellulose, agar, locust bean, pectin, tragacanth, and chitosan and gum karaya.

Celecoxib mainly used in Rheumatoid arthritis and severe pain during menstruation this drug is belonging to NSAIDS category.[1-9]

MATERIALS AND METHOD

Materials

Celecoxib was received as gift sample from Alembic Pharmaceutical ltd, Baroda. All other excipients were used of analytical grades.

Methods

The capsules were formulated using Wet granulation method. The composition of formulation is as given in Table 1.[10-11]

Evaluation[12-13]

Drug-Excipients Interaction Study was carried by using DSC

Dissolution Test

The *in vitro* drug release study was carried out using USP dissolution apparatus basket type apparatus. Speed of basket rotation was set on 75 rpm at temperature of $37^0 \pm 0.5^0$C. Samples were taken at the time interval of 5 min for 1 hour and analyzed by using UV spectrophotometer at λmax 275 and the dissolution profiles of test batches were compared with innovator's product.

Stability Study

The optimized formulation was charged for the accelerated stability studies according to ICH guidelines (40 ± 2ºC and 75 ± 5% RH) for a period of 3 months in a stability chamber.

The optimized formulations were placed in USP type-I flint vials and hermetically closed with bromobutyl rubber plugs and sealed with aluminum caps. The samples were withdrawn at 30, 60 and 90 days and evaluated for the drug content and In Vitro drug release.[14-15]

Table 1: Composition of nonsteroidal anti-inflammatory drug capsules (Batch F01-F08)

Sr no.	Ingredients (mg)	F01	F02	F03	F04	F05	F06	F07	F08
1	Celecoxib	400	400	400	400	400	400	400	400
2	Lactose monohydrate	65	65	65	65	65	40.3	57	30.3
3	SLS	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5
4	Povidone K90	12	12	12	12	12	12	-	-
5	Povidone K30	-	-	-	-	-	-	20	20
6	Purified water	Q.S.	-	-	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.
7	Acetone	-	Q.S.	Q.S.	-	-	-	-	-
8	SSG	25.3	25.3	25.3	-	-	-	-	-
9	Polyplasdone INF 10	-	-	-	-	25.3	-	-	-
10	Polyplasdone XL 10	-	-	-	25.3	-	-	25.3	26
11	Cross Carmellose Sodium	-	-	-	-	-	50	-	26
12	Magnesium stearate	5.2	5.2	5.2	5.2	5.2	5.2	5.2	5.2
	Total	520	520	520	520	520	520	520	520

RESULTS AND DISCUSSION

Drug-Excipients Interaction Study

The thermal behavior of the pure drug and the combination of drug and excipients was compared. The DSC trace of celecoxib showed endothermic peak between 271°C to 276°C as shown in figure 1 and 2 In the DSC trace of the mixture of API and excipients, the endothermic peak observed at same place in the majority of case. Melting endotherm of the drug was well preserved with a slight change in terms of broadening of peak or shifting towards the lower temperature. Thus these minor changes in the melting endotherm of drug could be due to the mixing of drug and excipients, which lowers the purity of each component in the mixture and may not necessarily indicating potential incompatibility.

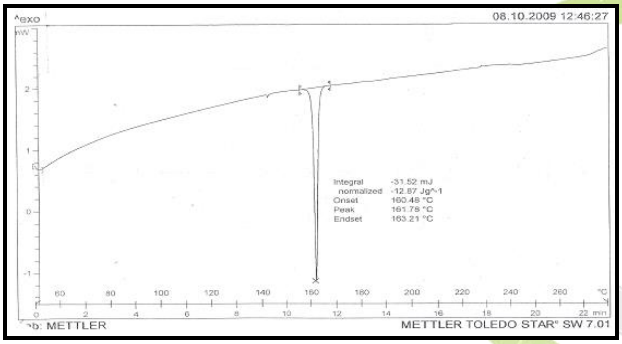

Figure 1: DSC graph of Celecoxib

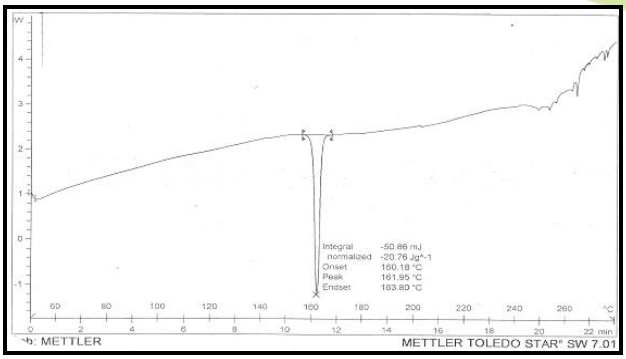

Figure 2: DSC graph of Celecoxib with all excipients

Dissolution

Dissolution was performed for different eight batches containing same active drug and the excipients but the main difference in the formulation is the disintigrants were different in each formulations. Each batch is showing different in vitro drug release compare to other that is shown in figure 3, 4 and 5.

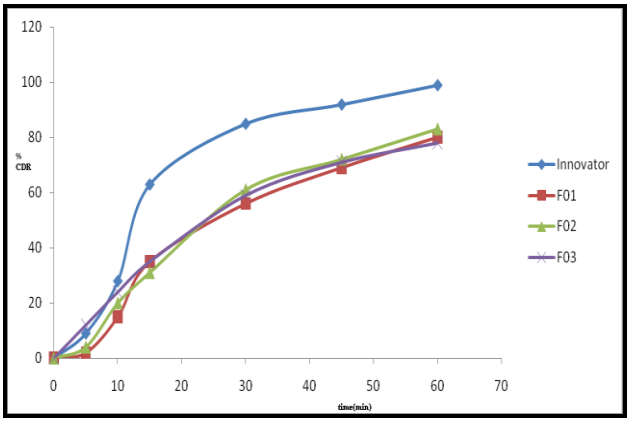

Figure 3: *In vitro* drug release for batch F01-F03

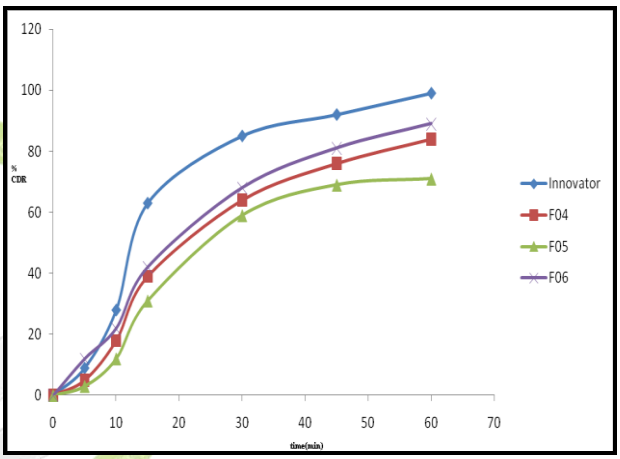

Figure 4: *In vitro* drug release for batch F04-F05

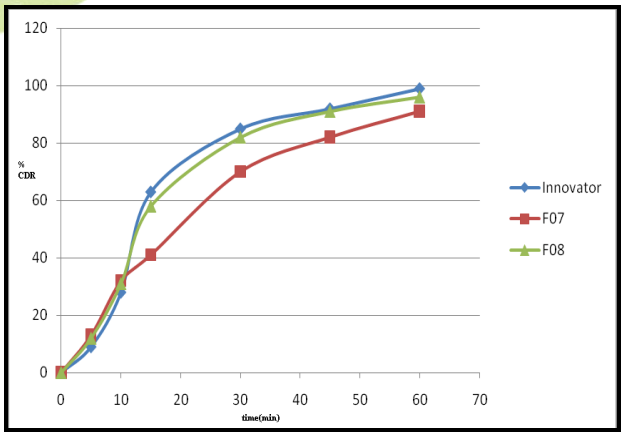

Figure 5: *In vitro* drug release for batch F07-F08

Stability Study

The optimized formulation was charged for the accelerated stability studies according to ICH guidelines (40 ± 2ºC and 75 ± 5% RH) for a period of 3 months in a stability chamber and

evaluated for different parameters as shown in table 2.

Table 2: Stability study

Parameters	Initial	1 Months	2 Months	3 Months
Assay (%)	98.7	98.8	101.7	98.3
Dissolution (%)	96.3	95.2	97.4	98.1
(30 min)	(95.6-97.2)	(93.8-96.3)	(96.3-97.9)	(97.7-99.4)

CONCLUSION

The study demonstrated that Celecoxib capsule prepared with various disintegrants prepared by wet granulation technique showed significantly higher dissolution in comparison with physical powder mixture having same drug excipients ratio. Out of the disintegrants studied Polyplasdone XL 10 grades were superior than the other disintegrants for the drugs studied and the combined effect of Polyplasdone XL 10 and cross Carmellose sodium gives better dissolution than individually. So ultimately combined effect of two disintegrants and low grade povidone K30 will give more than 80% dissolution within 30 min.

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REFERENCES

1. Chien, Y. W. Novel drug delivery systems. Marcel Dekker Inc, New York.
2. Lee, T. W., Robinson, J. R. (2001). Controlled-release drug-delivery systems Remington: the science and practice of pharmacy. Easton, Pennsylvania.
3. Aulton, M. E. (2002). Pharmceutics the Science of dosage form design Livingstone.
4. Lachman, L. (2010). The Theory and Practice of Industrial Pharmacy.
5. Lieberman, H. A., Lachman, L., Schwartz J.B. (2010). Pharmaceutical Dosage forms.
6. Raymond, C. R. (2003). Handbook of pharmaceutical excipients.
7. Augsgerger, L. L., & Hahm, H. A. (2010). *Superdisintegrants: characterization and function*, Encyclopedia of Pharmaceutical Technology.
8. Lin, S., & Lin, K. (1991). Influence of excipients, drug and osmotic agents in the inner core on the time controlled disintegration of compression coated ethyl cellulose tablets. *Journal of Pharmaceutical Science, 9,* 2040-2046.
9. Machelska, H., & Cabot, P. J. (1998). Pain control in inflammation governed by selecting. *Journal of Nature Medicine*, 17-25.
10. Goadsby P. J. (2000). The pharmacology of headache, *Progress in Neurobiology, 62*, 509-525.
11. Peatfield, R. C. (1995). Relationships between foods, wine, and beer-precipitated migrainous headaches, Headache.
12. Bayrak, Z., Tas, C. (2011). Formulation of zolmitriptan sublingual tablets prepared by direct compression with different polymers: In vitro and in vivo evaluation, European *Journal of Pharmaceutics and Biopharmacutics*, 499–505.
13. Shangraw, R. F., Direct Compression Tableting, *Encyclopaedia of Pharmaceutical Technology*, 1988.
14. Toti, U., Aminabhavi, T. (2004). Modified guar gum matrix tablet for controlled release of Diltiazem hydrochloride, *Journal of Controlled Release*, 95, 567-577.
15. Aulton, M. (1990). *Pharmaceutics the science of dosage form design*, 1st Ed, ELBS, Hongkong, 1990, 316.

