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TO COMPARE THE EFFECT OF SUPERDISINTEGRANTS IN THE FORMULATION OF TWO MODEL DRUGS FROM TWO DIFFERENT BCS CLASSES

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ABSTRACT

The proper choice of disintegrants or superdisintegrants and its consistency of performance are of critical task for formulation development. Most of papers published on the choice of superdisintegrant show varying results on the dissolution profile of drug. Hence, this research aimed in reasoning the effect of superdisintegrant on various drugs with respect to their solubility characteristics or their BCS classification. This study was conducted to explore the impact of superdisintegrant selection on the rate of dissolution of poorly soluble drugs. At a time when formulators are faced with increasing numbers of poorly soluble drugs, it has become very important to select superdisintegrants to maximize drug dissolution. For this purpose, superdisintegrants like Plantago ovata husk, Sodium Starch Glycolate [SSG], Crospovidone [CRP], Croscarmellose sodium [CCS], were studied on individual formulation of Diclofenac free acid and Aspirin. It was found that the relationship between disintegration time is dependent on the type of system and in particular the solubility characteristic of the entire system.

Keywords: Biopharmaceutical classification, solubility, Aspirin, Diclofenac, Superdisintegrant

INTRODUCTION

Dealing with such a classical item as solid dosage form, it could be observed that much work has been done in the superdisintegrant field. This is probably true, since most of the papers on the selection of superdisintegrant on specific drugs are reported earlier. **Nisha C Fernandes**, studied that effect of disintegrant in soluble matrices is lower than that in insoluble matrices.[1] **Na Zhao** and **Larry L. Augsburger** reported that Ac-Di-Sol was found to disintegrate tablets rapidly into primary particles compared to Primojel and Polyplasdone XL 10.[2] **Bhattu S.K., et.al.** reported that 6% Crospovidone was selected for Fenoverine tablets.[3] **Piera Di Martino et.al.** reported was better than Kollidon CL and Vivasol.[4] **Mulla J.A., et.al**. stated that Ac-Di-Sol was found to be better suited for the formulation of Promethazin.[5] **Setty Mallikarjna, et.al.** has studied the effect of functionality differences of the superdisintegrants on tablet disintegration by development of fast dispersible aceclofenac tablets with the use of Croscarmellose sodium, sodium starch glycolate and Crospovidone.[6] Santa**nu Chakraborty, et.al**., has studied Comparative study on effect of natural and synthetic Superdisintegrants in the formulation of fast dissolving tablets Natural super disintegrants like *Plantago ovata* mucilage showed better disintegrating property than the most widely used synthetic super disintegrants like SSG and Ac-di-sol in the formulations of FDTs. But on comparison these papers show varying results. Thus, the formulator has a difficulty in selecting these superdisintegrants on the drug of interest. Hence, work was done with the aim so that the choice of superdisintegrant would be easy.[7]

Material and Method:

Materials:

Plantago ovata laxmi brand husk was purchased from Rakesh Medical Store Shirpur, Dist Dhule, and Maharashtra. Diclofenac was obtained as gratis sample from **Micro Advanced Research Centre, Hurlu Bangalore**, **INDIA** and Aspirin from **Akhil Healthcare Pvt Ltd, Baroda Gujrat, INDIA**. Other materials used in the study were of pharmaceutical grade.

Method:

Different compositions were prepared as shown in (Table No.1) using different superdisintegrants. All the raw materials were weighed and then sifted through sieve no 80 to ensure better mixing. MCC was used as a direct compressible vehicle in the formulation. Superdisintegrants like SSG, Crospovidone, Ac-di-sol and husk of *Plantago ovata* were used in different proportions. All the

ingredients without magnesium stearate and talc were mixed uniformly followed by addition of magnesium stearate and talc. All these ingredients except magnesium stearate were mixed. Sifted magnesium stearate was then added to the blend and mixed. The blend was compressed on a 12 station compression machine (Rimek Mini Press-1) using 8 mm flat punches set.

Table No 1: Formulations of Diclofenac Containing different concentrations of different superdisintegrants.

Formulation	Diclofenac (mg)	Husk[a] (mg)	Ac-di-Sol[b] (mg)	CP[c] (mg)	SSG[d] (mg)	MCC[e] (mg)	Mannitol (mg)	Sod. Saccharine (mg)	Talc (mg)	Mg. Sterate (mg)	Total Weight (mg)
A0	50	-	-	-	-	100	34	10	4	2	200
AN1	50	12	-	-	-	100	22	10	4	2	200
AN2	50	16	-	-	-	100	18	10	4	2	200
AN3	50	20	-	-	-	100	14	10	4	2	200
AA1	50	-	12	-	-	100	22	10	4	2	200
AA2	50	-	16	-	-	100	18	10	4	2	200
AA3	50	-	20	-	-	100	14	10	4	2	200
AP1	50	-	-	12	-	100	22	10	4	2	200
AP2	50	-	-	16	-	100	18	10	4	2	200
AP3	50	-	-	20	-	100	14	10	4	2	200
AS1	50	-	-	-	12	100	22	10	4	2	200
AS2	50	-	-	-	16	100	18	10	4	2	200
AS3	50	-	-	-	20	100	14	10	4	2	200

[a]Plantago ovata husk ,[b]AC-di-Sol, [c]Crospovidone,[d]Sodium starch glycolate,[e]Microcrystalline cellulose

EVALUATION:

1. Uniformity of weight: The weight of 20 from tablets was analyzed for sample mean and standard deviation.

2. **Hardness**: For each formulation, the hardness of tablets was determined using the Monsanto hardness tester.

3. **Thickness**: For each formulation thickness of tablets was determined by Vernier caliper (Mitutuyo 99MAC002M5).

4. Friability: It was calculated from the weight loss of tablets tumbled at 100 revolutions in Electrolab Friabilator (USP) model: EF – 1W.

Table No 2: Formulations of Aspirin Containing Different Concentrations Of Different Superdisintegrants.

Formulation	Aspirin (mg)	Husk[a] (mg)	Ac-di-Sol[b] (mg)	CRP[c] (mg)	SSG[d] (mg)	MCC[e] (mg)	Mannitol (mg)	Sod. Saccharine	Talc (mg)	Mg. Sterate (mg)	Total Weight (mg)
A0	81	-	-	-	-	69	34	10	4	2	200
AN1	81	12	-	-	-	69	22	10	4	2	200
AN2	81	16	-	-	-	69	18	10	4	2	200
AN3	81	20	-	-	-	69	14	10	4	2	200
AA1	81	-	12	-	-	69	22	10	4	2	200
AA2	81	-	16	-	-	69	18	10	4	2	200
AA3	81	-	20	-	-	69	14	10	4	2	200
AP1	81	-	-	12	-	69	22	10	4	2	200
AP2	81	-	-	16	-	69	18	10	4	2	200
AP3	81	-	-	20	-	69	14	10	4	2	200
AS1	81	-	-	-	12	69	22	10	4	2	200
AS2	81	-	-	-	16	69	18	10	4	2	200
AS3	81	-	-	-	20	69	14	10	4	2	200

[a] Plantago ovata husk,[b]AC-di-Sol,[c] Crospovidone,[d] Sodium starch glycolate,[e] Microcrystalline cellulose

5. Swelling Index

Swelling index (British Pharmacopoeia Vol. II, 1988) is the volume in milliliters that is occupied by 1 gm of drug or any adhering mucilage after it has swollen in an aqueous liquid for 4 h. The methods of studying swelling index for *Plantago ovata*, Crospovidone, SSG and Ac-di-sol were carried out as per BP specifications. Swelling index was calculated from mean readings of three determinations (Table No.3).

Table No.3 swelling index of different superdisintegrants

S.No.	Name of superdisintegrants	Swelling Index (%v/v)
1	*Plantago ovata*	92±2.0
2	Cross Carmellose sodium	68±1.8
3	Crosspovidone	56±1.5
4	Sodium starch glycolate	48±1.2

Values are expressed as Mean ±S.D[a]. n=3. [a] Standard deviation.

6. Disintegration Time: It was performed at 37ºC in water using ELECTROLAB EL – 2L without disks.

Experimental Design:

Formulations containing superdisintegrants (Sodium Starch Glycolate, Crospovidone, Croscarmellose sodium, and Plantago ovata husk) in their concentration varying from 6, 8 and 10% were formulated. This experiment aimed at determining the effect of superdisintegrant addition on separate formulations with 2 model drugs based on different BCS classes. For this purpose three model drugs (a representative of the respective classes) such as Diclofenac free acid (Class II) and Aspirin (Class III) were studied for superdisintegrant effect on disintegration time. (Table 1)

RESULT AND DISCUSSION:

At 6, 8, 10% concentration of superdisintegrant, there was a trend that the D.T. of Diclofenac free acid was low. But Aspirin showed an exuberant D.T. The most important parameter that needs to be optimized in the development of fast dissolving tablets is the disintegration time of tablets.

In the present study, all the tablets disintegrated in ≤3 min fulfilling the official requirements for dispersible tablets. It is observed that the disintegration time of the Diclofenac tablets decreased (from 16 to 8 sec) with increase in the level of superdisintegrant from 6% to 10% (Fig.No1,2,3).

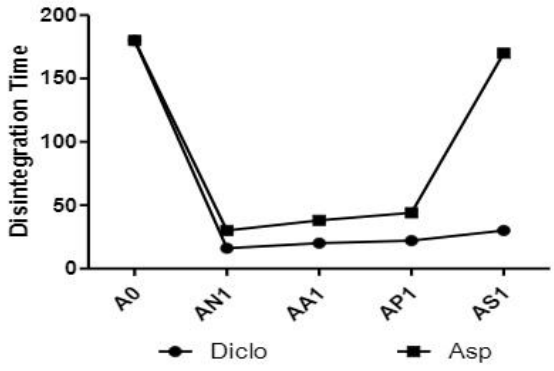

Fig. 1: Effect of drug solubility on D.T. of 6% superdisintegrants. Diclo-Diclofenac, Asp-Aspirin, A0-Formulation without the superdisintegrant, AN1- Formulation with the 6% Plantago ovata husk, AA1-- Formulation with the 6% Ac-di-Sol.AP1- Formulation with the 6% Crospovidone, AS- Formulation with the 6% Sodium starch glycolate.

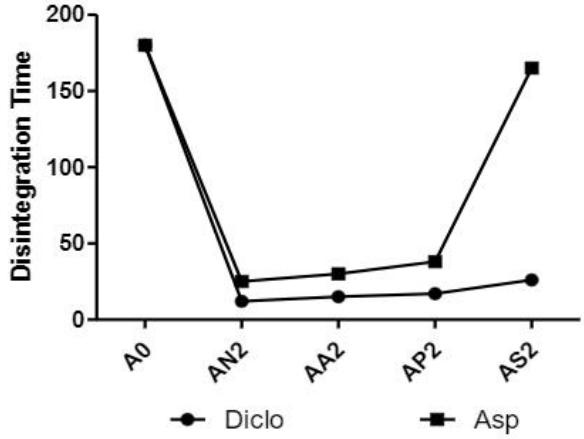

Fig.No. 2: Effect of drug solubility on D.T. of 8% superdisintegrants. Diclo-Diclofenac, Asp-Aspirin, A0-Formulation without the superdisintegrant, AN2- Formulation with the 8% Plantago ovata husk, AA2-- Formulation with the 8% Ac-di-Sol, AP2- Formulation with the 8% Crospovidone, AS2- Formulation with the 8% Sodium starch glycolate.

Fig.No. 3: Effect of drug solubility on D.T. of 10% superdisintegrants. Diclo-Diclofenac, Asp-Aspirin, A0-Formulation without the superdisintegrant, AN2- Formulation with the 10% Plantago ovata husk, AA2-- Formulation with the 10% Ac-di-Sol, AP2- Formulation with the 10% Crospovidone, AS2- Formulation with the 10% Sodium starch glycolate.

The disintegration time of Aspirin decreased (from 30 to 15 sec) with increases in the level superdisintegrant with similar concentration. The effect of disintegrate in Aspirin matrices is lower than that in Diclofenac matrices. Tablets containing high concentrations of water soluble drug, drugs normally tend to erode, rather than disintegrate, which may result in slow disintegration. Selecting formulation ingredients that enhance the dissolution of poorly soluble drugs has therefore become increasingly important to achieve therapeutic efficacy. Once a tablet disintegrates, the solubility properties of the drug, either alone or assisted by other formulation ingredients, determine the drug's subsequent dissolution rate and extent of release. Aspirin, though it is highly soluble, the entire system tries to first take up the water, trying to dissolve rather than disintegrate. Diclofenac free acid however, tries to disintegrate as soon as possible.

CONCLUSION:

It was seen that Diclofenac free acid (II) being insoluble, shows very less disintegration time. Aspirin (III) being soluble shows high disintegration time. Diclofenac free acid however, tries to disintegrate as soon as possible. Thus, it was found that the relationship between disintegration time is dependent on the type of system and in particular the solubility characteristic of the entire system. It was observed that for direct compression, irrespective of the drug class.

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