Research Article **CODEN: IJRPJK** **ISSN: 2319 – 9563**

International Journal of Research in Pharmaceutical and Nano Sciences

Journal homepage: **www.ijrpns.com**

COMPARATIVE EVALUATION OF DISITEGTRANT PROPERTIES IN NIMESULIDE TABLET FORMULATION BY USING NATURAL AND SYNTHETIC SUPERDISINTEGRANT

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ABSTRACT

The main objective of the present investigation was to study comparative evaluation of nimesulide tablet formulation by using different superdisintegrants. In this comparative study were developed two types of superdisintegrant one is the natural like maize starch and potato starch another is the synthetic superdisnterant like sodium starch glycolate and microcrystalline cellulose. The tablets of the nimesulide were prepared by direct compression technique. The prepared tablets evaluated in terms of their pre-compression studies, post-compression studies and in vitro study and release kinectic study. The Disitegration study and *Invitro* study showed that formulation of natural superdisintegrant gives better result than the synthetic superdisintegrants.

KEYWORDS

Nemisulide, Maize starch, Potato starch, Sodium starch glycolate, Microcrystalline cellulose, and *In vitro* study.

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INTRODUCTION

Oral fast release dosage form by direct compression technique is a very simple approach in pharmaceutical area preparation of tablet it is ease, compliance, faster, production, avoid hydrolytic and oxidation reaction occurred during processing of dosage form. The oral route is the most favorable route for administration of drugs because of accurate dosage, lowest cost to the therapy, *self*-administers treatment of medication, non-invasive method and easy administration gives to patient high level compliance. Of the oral dosage forms, solid dosage form is the preferred class of product

as tablet represents a unit dosage form in which one dose of drug is placed accurately[1].

'Fast Dissolve', 'Quick Dissolve', 'Rapid Melt', 'Quick Disintegrating', 'Mouth Dissolving', 'Orally Disintegrating tablet ', 'Oral Dispersible', 'Melt-In-oral cavity', etc. are terms that forms the same drug delivery system. Recently orally disintegrating (OD) tablet technology has been approved by standard pharmacopeia that is (USP) and (CDER) .USFDA defined OD tablet as "a solid dosage form containing medical substances, which disintegrates fastly, usually within few second, tablet taken in the tongue". In the European pharmacopoeia also adopted the term "oro-dispersible tablets" as a tablet that is to be placed in the mouth where it disperses rapidly before swallowing[2].

The dosage forms dissolve or disintegrate in the patient's mouth within 15 seconds to 3 minutes without the need of water or chewing. As that of above also give other terminology; oral-dispersible tablets are here to offer equal form of drug delivery with many advantages over the conventional oral solid dosage forms[3]. The perfect quality of Superdisintegrants and its consistency of performance are of interpretative importance to the formulation development of these tablets. In more recent years, increasing observations towards formulating not only fast dissolving tablet and disintegrant tablet that are swallowed, but also orally disintegrating tablets that are intended to dissolve and/or disintegrate rapidly in water and to be swallowed[4]. Superdisintegrants are more effective at lower concentrations with greater Disintegrating efficiency and mechanical strength. On contact with water the superdisintegrants swell, hydrate, change volume or form and produce a disruptive change in the tablet[5]. Effective superdisintegrants provide improved compatibility and have no negative impact on the mechanical strength of tablet formulation which containing more amount of dose drugs, some commonly used superdisintegrants are cross linked carboxyl methyl cellulose (Croscarmellose), sodium starch glycolate, polyvinylpyrroli done etc[6].

In present investigation attempt is made to study the effect of varying concentration of various natural and synthetic superdisintegrants on the tablet performance.

Nimesulide is a non-steroidal and anti-inflammatory drug, in the market more than 50 countries referred these categories of drug. Reports of safety and tolerability of nimesulide are available as descriptive reviews, case reports and post marketing surveillance trials[7]. Direct compression is the preferred method for the preparation of tablets[8]. It offers several advantages[9,10]. Notable among them are (i) It is economical comparing to the wet granulation it requires few unit operations (ii) More suitable for moisture and heat sensitive APIs since it eliminates wetting and drying steps (iii) Changes in the dissolution profiles are less to occur in tablets made by direct compression method on storage than in those made from granulations[11]. This is extremely important because the official compendium now requires dissolution specifications in most solid dosage forms[12].

MATERIAL AND METHODS

Material

Nimesulide was obtained from Alembic Pvt. Ltd; Vadodara. Maize starch, potato starch, sodium starch glycolate, microcrystalline cellulose and Avicel PH 102 were a Gift sample from Loba Chemic Mumbai. All other chemicals and ingredients were used for study are of Analytical grade.

Methods[13-17]

The composition of formulations of Nimesulide fast disintegrant tablets is shown in Table No.1. All the powders passed through 40/60 mesh sieve. The required quantity of pure drug and superdisintegrant and other ingredients were mixed thoroughly then add Talc and magnesium stearate were finally added as a Avicel PH 102 respectively. The blend was directly compressed by KBr Press Each tablet containing 100 mg of pure Nimesulide.

EVALUATION PARAMETERS

Pre-formulation Studies

Fourier Transform Infrared Spectroscopy[18]

The fourier transform infra-red analysis was conducted for the structure characterization FTIR spectra of the pure drug Nimesulide. Approximately 5mg of samples were mixed with 50mg of spectroscopic grade KBr, samples were scanned in the IR ranges found 500 to 2000 cm-1, with a resolution of 4 cm-1.

Preliminary studies of fast disintegrant tablet granules

Bulk density[19]

It is ratio of total mass of powder to the bulk volume of powder which is the placed in the measuring cylinder and volume was noted as bulk density (Db)

It expressed in gm/cc and is given by: Db =M/Vb

Where, M= is the mass of powder.

Vb= is the bulk volume of powder.

Tapped Density[19]

It is the ratio of total mass of powdered to the tapped volume of powder. The tapped volume was measured by tapping the powder to a constant volume.

It is expressed in gm/cc and is given by: Dt =M/Dt

Where, M= is the mass of powder.

Vt = is the tapped volume of the powder.

Hauser Ratio[20]

Hausner Ratio is an indirect index of ease of powder flow. It is calculated by the following formula:

Hausner Ratio =Dt/Db

Where, Dt = Tapped density

Db = Bulk density

Hausner Ratio value of powder show in table

Swelling index[21]

The study was carried out using a 100 ml stoppered graduated cylinder .The initial bulk volume of 1 gm of starch was noted water was added in sufficient quantity of water to produce 100 ml of a uniform dispersion and was stored at room temperature and the sediment volume of the swollen mass was measured after 24 hour.

Carr's index (I) [21]

It indicates the ease with which a material can be induced to flow. It is expressed as a percentage and is given by

Carr's index (%) = (Tapped density –Pour density)/Tapped densityX100

Carr's index values of powder show in table

Angle of repose (θ) [22]

The frictional force in a loose powder can be measured by the angle of repose. It is defined as maximum angle possible between the freely sliding surface of a pile of powder and the horizontal plane.

$$\text{Tan } \theta = \tan^{-1}(h/r)$$

Where, θ = is the angle of repose

h=is the height

r =is the radius

Flow properties and corresponding angle of repose.

POST-COMPRESSION STUDIES NIMESULIDE FAST DISINTEGRANT TABLETS

Hardness or Crushing strength Test[22]

Hardness of the tablet was determined using the Monsanto hardness tester. The lower plunger was placed in contact with the tablet and a zero reading was taken. The plunger was then forced against a spring by tuning a threaded bolt until the tablet damaged. The force required to break the tablet is measured in kilograms and a crushing strength it will found in near to 4Kg is usually considered as satisfactory tablets. For oral tablets normally have a hardness of 4 to 10 kg; however, hypodermic and chewable tablets have a hardness of 3 kg and some sustained release tablets have a hardness of 10-20 kg.

Thickness Test[23]

The thickness of the tablet is mostly related to the tablet hardness can be uses as sartig parameter is to be selection of tablets were randomly and then from each tablet thickness was determined using a Vernier calliper and the reading was recorded in millimeters.

Friability Test[24]

The pre-weighed tablets were placed in the friabilator (EF-2, Electro lab, Mumbai) which was

then operated for 100rpm, then dusted and reweighed. The Conventional compressed tablets that lose less than 0.5-1.0% of their weight are generally considered acceptable.

Friability index =I-F/IX 100

Where,

I - Initial weight, F - Final weight

Weight variation test[24]

Weights of 20 individual tablets are taken and also mean weight of tablet also calculate. The percentage deviation was calculated by using the following formula,

Percentage deviation = [X-X*/ X] × 100

X - Actual weight of the tablet,

X*- Average weight of the tablet

Estimation of Drug Content[25]

An accurately weighed amount of powdered nimesulide (100 mg) was extracted with water and the solution was filtered through 0.45 µ membrane filter paper and absorbance was measured at 275 nm after dilution.

Calculation

The amount of Aceclofenac present in tablet can be calculated using the formula

At/As x Sw/100 x 100

Where,

At = Absorbance of sample preparation,

As = Absorbance of Standard preparation,

Sw = weight at Aceclofenac working standard (mg)

***In vitro* Drug Release Studies**[26-28]

The *in vitro* drug release study was carried out for 24 hours using USP paddle type dissolution test apparatus in phosphate buffer (pH 6.8) at 75 rpm maintaining temperature at 37±0.50c. A 10ml of samples were collected from each vessel at 0, 2, 4, 8, 12, 16 and 24 hours and analyzed by UV spectrophotometer at 275 nm. The withdrawn sample was immediately replaced by equal volume of fresh buffer. The dissolution data obtained were plotted as percentage drug release versus time and calculate the drug release of tablet.

***In Vitro* Disintegration**[29-32]

Six tablets of each formulation used to determine disintegration time. Phosphate buffer (pH 6.8) was used as a disintegration medium and temperature was maintained 37±0.50C. Average disintegration time of six tablets was determined. Phosphate buffer Media volume 900 ml.

RESULTS AND DISCUSSION

Table No.1: Formulation of different batches of Nimesulide Fast Disintegrant Tablets (mg/tab)

S.No	Ingredients (mg)	SSG1	SSG2	SSG3	MCC1	MCC2	MCC3	PS1	PS2	PS3	MS1	MS2	MS3
1	Nimesulide	100	100	100	100	100	100	100	100	100	100	100	100
2	Sodium Starch Glycolate	5	10	15	-	-	-	-	-	-	-	-	-
3	Microcrystalline cellulose	-	-	-	5	10	15	-	-	-	-	-	-
4	Potato starch	-	-	-	-	-	-	5	10	15	-	-	-
5	Maize starch	-	-	-	-	-	-	-	-	-	5	10	15
6	Avicel PH 102	140	135	130	125	140	135	130	125	140	135	130	125
7	Talc	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
8	Magnesium Stearate	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
9	Total	250	250	250	250	250	250	250	250	250	250	250	250

Table No.2: Angle of Repose I.P limits

S.No	Angle of repose	Flow property
1	25-30	Excellent
2	31-35	God
3	36-40	Fair
4	41-45	Passable
5	46-55	Poor
6	56-65	Very Poor
7	>66	Very, Very Poor

Table No.3: Carr's Index I.P limits

S.No	Carr's index (%)	Type of flow
1	5-15	Excellent
2	12-18	Good
3	18-23	Fair to passable
4	23-35	Poor
5	35-38	Very poor
6	>40	Extremely poor

Table No.4: Hausner's Ratio I.P Limits

S.No	Hausner's Ratio	Type of flow
1	<1.25	Good
2	1.25-1.5	Moderate
3	>1.5	Poor

Table No.5: Pre-compression studies of Nimesulide Fast Disintegrant granules

S.No	Properties	Sodium Starch Glycolate	Micro Crystalline Cellulose	Potato Starch	Maize Starch
1	Bulk Density	0.4761	0.4347	0.6666	0.4761
2	Tapped Density	0.6250	0.5555	0.8333	0.6250
3	Hausner's Ratio	1.3127	1.2718	1.2500	1.3127
4	% Carr's Index	23.8240	21.7461	20.0048	23.8240
5	Angle Of Repose	27.68^0	25.59^0	28.30^0	28.75^0

Table No.6: Post-compression studies of Nimesulide Fast Disintegrant Tablets

S.No	CODE	Thickness (mm)	Diameter (mm)	Weight Variation	Hardness (kg/cm)	Friability (%)	Tensile Strength	Water Abs. Ratio	DT* (sec)
1	SSG1	0.540	0.816	Complies	2.10	0.8974	3.0656	65.92	42
2	SSG2	0.520	0.813	Complies	2.23	0.8438	3.3787	65.89	49
3	SSG3	0.520	0.820	Complies	2.26	0.7083	3.4242	66.82	55
4	MCC1	0.540	0.816	Complies	2.11	0.8974	3.0656	65.92	44
5	MCC2	0.520	0.813	Complies	2.22	0.8438	3.3787	65.89	51
6	MCC3	0.520	0.820	Complies	2.30	0.7083	3.4242	66.82	56
7	PS1	0.540	0.816	Complies	2.13	0.8974	3.0656	65.92	50
8	PS2	0.520	0.813	Complies	2.21	0.8438	3.3787	65.89	56
9	PS3	0.520	0.820	Complies	2.25	0.7083	3.4242	66.82	60
10	MS1	0.540	0.816	Complies	2.12	0.8974	3.0656	65.92	59
11	MS2	0.520	0.813	Complies	2.22	0.8438	3.3787	65.89	61
12	MS3	0.520	0.820	Complies	2.26	0.7083	3.4242	66.82	66

Table No.7: Release kinetics

Release kinetics							
S.No	**Formulation**	**Zero order r2**	**First order r2**	**Higuchi r2**	**Hixsoncrowell r2**	**Korsmeyer -Peppas r2**	**N (Slope)**
1	PS1	0.948	0.92	0.914	0.938	0.94	0.509
2	PS2	0.977	0.969	0.949	0.979	0.952	0.574
3	PS3	0.965	0.961	0.933	0.97	0.923	0.529
4	MS1	0.972	0.982	0.963	0.982	0.952	0.686
5	MS2	0.972	0.952	0.919	0.958	0.919	0.693
6	MS3	0.964	0.926	0.91	0.943	0.931	0.558
7	SSG1	0.986	0.991	0.979	0.995	0.974	0.717
8	SSG2	0.977	0.945	0.915	0.959	0.907	0.618
9	SSG3	0.963	0.943	0.917	0.957	0.918	0.530
10	MCC1	0.963	0.951	0.962	0.984	0.952	0.546
11	MCC2	0.962	0.9532	0.925	0.935	0.921	0.520
12	MCC3	0.966	0.954	0.935	0.955	0.963	0.522

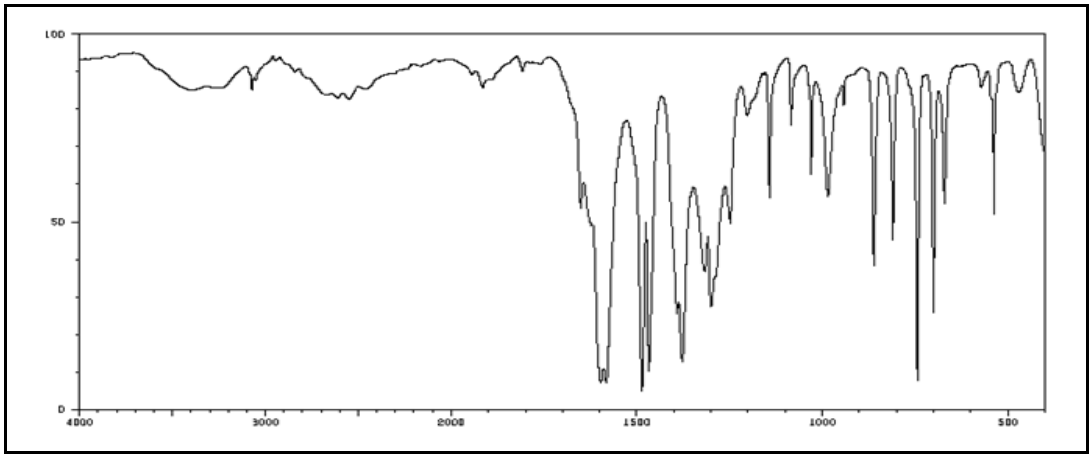


Figure No.1: IR Spectrum of Nimesulide Pure Drug

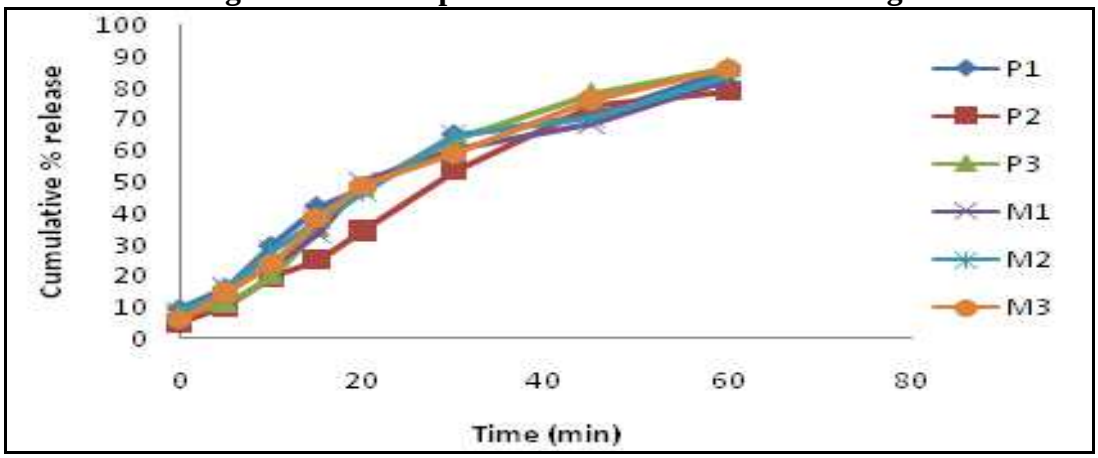


Figure No.2: *In-vitro* drug release profile of fast disintegrating tablet of Nimesulide contains Potato Starch (P1, P2 and P3) and Maize starch (M1, M2 and M3)

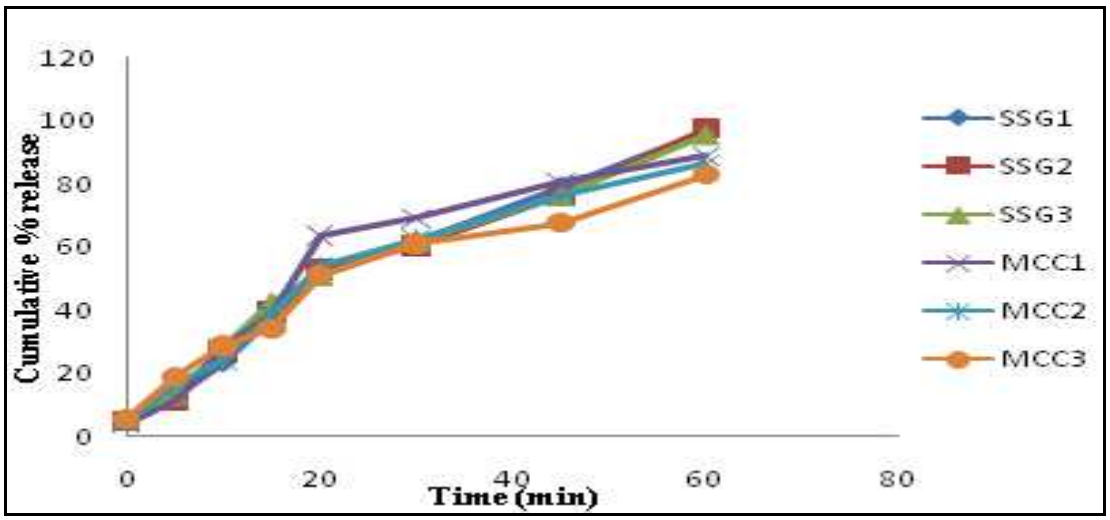
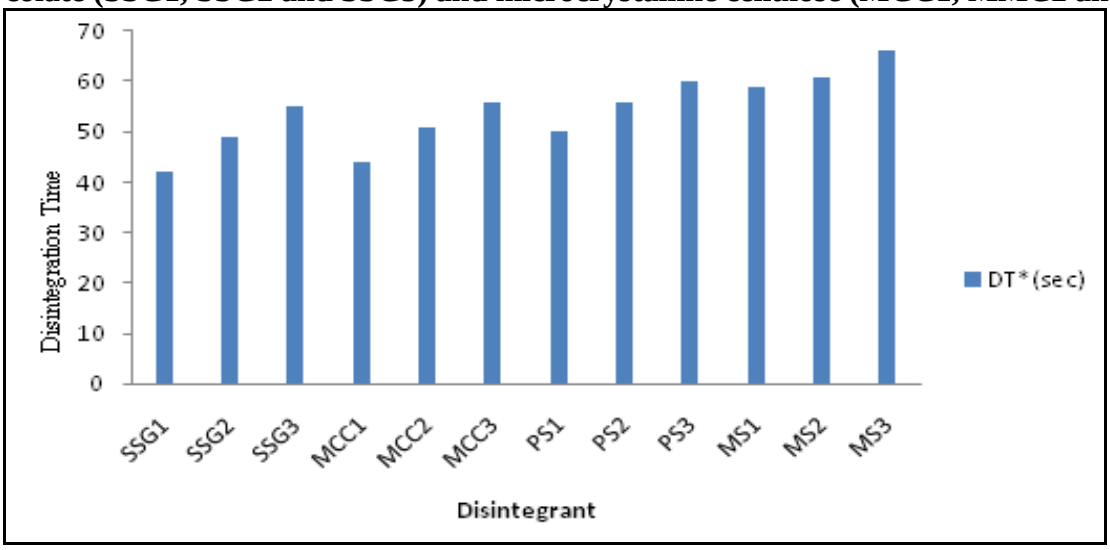


Figure No.3: *In-vitro* drug release profile of fast disintegrating tablet of Nimesulide contains sodium starch glycolate (SSG1, SSG2 and SSG3) and microcrystalline cellulose (MCC1, MMC2 and MCC3)



Graph No.1: Comparative evaluation of tablet of Nimesulide contains Sodium Starch Glacolate (SSG1, SSG2 and SSG3), Microcrystalline cellulose (MCC1, MCC2 and MCC3), Potato Starch (PS1, PS2 and PS3) and Maize starch (MS1, MS2 and MS3) Disintegrant on disintegration time

CONCLUSION

The Fast disintegrating tablets of Nimesulide were successfully formulated by direct compression technique. The Fast disintegrating tablets of Nimesulide containing natural and synthetic superdisintegrant showed satisfactory results more than 60min and the drug release of sodium starch glycolate has better release of drug when it is compared to other kinectic study shows the .

ACKNOWLEDGEMENT

The authors are sincerely thanks to the Gourishankar Institute of Pharmaceutical Education and Research, Limb, Satara, India for providing the facilities to complete this research work.

CONFLICT OF INTEREST

We declare that we have no conflict of interest

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Please cite this article in press as: Gharge Varsha G *et al.* Comparative evaluation of disitegtrant properties in nimesulide tablet formulation by using natural and synthetic superdisintegrant, *International Journal* of *Research in Pharmaceutical and Nano Sciences,* 6(1), 2017, 1-9.