

# Starch-silicon dioxide coprecipitate as superdisintegrant: formulation and evaluation of fast disintegrating tablets

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## Abstract

The objective of the present investigation is to synthesize and characterize starch-silica coprecipitate and evaluate as tablet superdisintegrant. The starch-silica coprecipitate was synthesized by coprecipitation of silica on the surface of starch particles as reported by Rashid et al. The coprecipitate was characterized in terms of compressibility characteristics, Differential Scanning Calorimetry (DSC) and Fourier Transformed Infra Red Spectroscopy (FTIR). Fast dissolving tablets were then formulated by direct compression method using the different concentration of coprecipitate, crosscarmellose sodium (CCS) and crosspovidone (CP) as superdisintegrant. The tablets were evaluated for the disintegration time, hardness, friability, tensile strength, weight variation and in vitro release studies. The starch-silica coprecipitate showed better disintegration and compressibility characteristics as compared to the known superdisintegrants. FTIR indicated the absence of any chemical reaction between the two species (starch and silica) during the process of coprecipitation. DSC studies showed there is no interaction between the drug and coprecipitate. Hausner's ratio & Carr's index value of (1.17 and 14.7 respectively) of coprecipitate suggested excellent flowability. The coprecipitate was found to be effective at all the concentrations tested in the fast dissolving tablet formulation. Disintegration time (DT) of less than 30 seconds was observed in case of coprecipitate whereas higher DT values was observed with CCS and CP as superdisintegrants. Starch-silica coprecipitate can be utilized as a superdisintegrant in the pharmaceutical applications owing to better compressibility and release characteristics.

**Keywords:** Coprecipitate, crosspovidone, Crosscarmellose sodium, flowability, compressibility, disintegration time.

## Introduction

The focus on drug development costs is driving the industry to consider outsourcing, relocating production and sourcing ingredients from lower-cost locations. The major area of potential is the innovative, new excipients offered by various excipient suppliers enable the development of new dosage forms, improve efficiency and may reduce the cost of drugs. They offer opportunities to introduce new dosage forms, and thus facilitate the extension of patent life. The novel excipients include excipients for direct compression, fast dissolving tablets and controlled release etc [1]. Microcrystalline Cellulose (MCC) is the most useful filler/binder for direct compression. MCC also has some disintegrant and anti-adherent properties. Many MCC based, co-processed excipients with improved functional properties such as compressibility and flowability have been studied [2]. Fast dissolving tablets are formulated to eliminate the swallowing difficulty and unpalatable taste which is primary limitation of the

conventional formulations [3, 4]. The most common and simple approach used in the formulation of the orally disintegrating tablets is the use of superdisintegrants [5, 6]. Disintegrating agents promote the breakup of the formulation into smaller fragments. They should have poor solubility, poor gel formation, good hydration capacity and good molding and flow properties [7-10]. Starch is the most widely used disintegrant in the pharmaceutical industry and used in higher concentration for effective disintegration [10-11]. Superdisintegrants are used in the very small amount for rapid disintegration as they swell several times of their original size when placed in water while producing minimal viscosity effects [12]. Most widely used superdisintegrants are crosscarmellose, crosspovidone, and sodium starch glycolate. The major mechanisms for disintegration are swelling of disintegrant (most common in tablet disintegration), porosity, capillary action and chemical reaction [13-14]. But there are some of the limitations in the use of conventional superdisintegrants such as decrease in the liquid uptake rate of the sodium starch glycolate



and crosscarmellose sodium in the acidic medium and decrease in the degree of swelling of sodium starch glycolate and crosspovidone by the use of wet granulation method [15-17]. Efforts in the direction of novel excipients led to the development of chitosan-silicon dioxide coprecipitate and PVP crosslinked with glutaraldehyde as novel superdisintegrants with improved compressibility and compactability characteristics and optimal tableting properties[18, 19]. The present study was intended to prepare coprecipitate of silicon dioxide and starch with the aim to explore industrial potential of starch as superdisintegrant over the conventional superdisintegrants. The coprecipitate was analyzed for surface characterization and flow properties. Starch-Silica coprecipitate was then incorporated in fast dissolving tablets using Nimesulide as model drug and evaluated for in vitro drug release in comparison with existing superdisintegrants (Crosspovidone and Cross carmellose sodium).

## Material and Methods

### Materials

Nimesulide, Cross carmellose sodium and Cross povidone were received as gift samples from Park Pharmaceuticals, Baddi, India. Starch and silicon dioxide were kindly gifted by Helios Pharmaceuticals, Baddi, India. Talc and magnesium stearate were purchased from S. D. Fine Chemicals Ltd. Mumbai, India. All other chemicals and reagents were of analytical grade and were used as such.

### Methods

#### Preparation of Starch-Silica Co-precipitate

The coprecipitate was prepared by the method as reported by Rashid et al. Starch (50 g) was dispersed in 100 mL of 2 M hot (80°C) HCl solution for 1 hr. Colloidal silicon dioxide (50 g) was dispersed in 100 mL of 2M NaOH solution to which 100 mL of distilled water was added under stirring until homogenization of the silica suspension was accomplished. The starch suspension was added gradually to the silica suspension at an approximate rate of 100 mL/min under vigorous stirring which was proceeded for 1 hr at ambient temperature (25°C) after completion of addition. The pH of the mixture was kept not to exceed, through mixing, a pH range from 6.5 to 7.0 by adjustment with concentrated HCl. The product was washed with deionized water. Then the product was filtered out using 20–25 mm filter papers. The filtrate solution was clear as starch and/or silica particles cause turbidity when present. The product was filtered out, dried in the oven at 90°C, and finally passed over a mesh of 425 mm size and kept for further testing and characterization of the obtained material.

## Evaluation of physical properties of co-precipitate

### Bulk density ( $D_b$ ) and Tapped density ( $D_t$ )

It is the ratio of total mass of powder to the bulk volume ( $V_b$ ) of powder. It was measured by pouring the weighed powder ( $M$ ) into a measuring cylinder and initial weight was noted.

Tapped density is the ratio of total mass of the powder to the tapped volume of the powder. Tapped volume was measured by tapping the powder for 100 times.

### Carr's Compressibility Index (I)

It is expressed in percentage and is given by

$$I = \{(D_t - D_b) / D_t\} * 100$$

Where,  $D_t$  is the tapped density of the powder and  $D_b$  is the bulk density of the powder

### Hausner Ratio

Hausner ratio is an indirect index of ease of powder flow. It is the ratio of tapped density to bulk density. Lower hausner ratio (<1.25) indicates better flow properties than higher ones (>1.25).

## Characterization of Starch-Silica Coprecipitate

### Scanning Electron Microscopy (SEM)

The surface morphology of the starch and silica particles was observed by the Scanning Electron Microscopy (SEM) (JSM. 6600, Jeol, Japan). Starch and Starch-Silica coprecipitate samples were mounted on Aluminium stubs and then coated with gold by sputtering at 1200 V, 20 Ma for 105 s using a vacuum coater.

### FTIR Spectroscopy

Infrared spectroscopy was used to follow the molecular interaction between starch and silica. Samples of starch, silica, starch-silica coprecipitate, physical mixture of starch and silica at the mass ratio of 1:1 were mixed with dried KBr (1% w/w). Then a small portion of the mixture was compressed in a special die at 15000 pounds per square inch to yield a transparent disk. The disk was then held in the instrument beam for spectroscopic examination.

### X-Ray Diffraction

The XRD patterns of starch-silica coprecipitate, starch, and silica were measured using X-ray diffractometer (X-pert PRO, Panalytical, Netherland) using Ni-filtered, CuK radiation, with a voltage of 40kV and 25mA current. The scanning rate employed was 10 min<sup>-1</sup> over a 10 to 30° diffraction angle (2  $\theta$ ) range.

### Differential Scanning Calorimetry

The DSC thermograms of the samples were obtained using Differential Scanning Calorimetry (DSC Q10V9.9 Build 303). Samples were sealed in 40 $\mu$ L aluminium pans. An identical empty

pan was used for the reference purpose. Nimesulide was physically mixed with Starch-Silica at the mass ratio of 1:1 and the mixtures were subjected to DSC studies. The scanning was performed under atmospheric conditions. A heating rate of 10°C/min was used for all samples.

### Formulation of Tablets by Direct Compression Method

Nimesulide is used as a model drug for the formation of all batches of tablets. Twelve batches (B1-B12) of the fast disintegrating tablets were prepared by using crosscarmellose sodium, croscopolvidone and starch-silica coprecipitate as superdisintegrants at different concentrations (1%, 5%, 10% and 20%), avicel as a filler and magnesium stearate as lubricant by direct compression method. The composition of the different batches is depicted in Table 1.

### Physicochemical evaluation of tablets

#### Disintegration Time

Disintegration test of the tablet was measured by USP disintegration test apparatus, in water (37±2°C). Time in seconds was noted until complete disintegration of tablet.

#### Weight Variation test

Weight variation test was done as specified in official standards.

#### Hardness

Hardness of the tablet was measured by using the Monsanto tablet hardness tester. It is expressed in kg/cm<sup>2</sup>.

#### Tensile Strength

The tensile strength is the force required to break a tablet by compressing it in the radial direction and is measured using a Monsanto hardness tester. Tensile strength for crushing (T) is calculated using equation:

$$T = 2F / dt$$

Where F is the crushing load, and d and t signify the diameter and thickness of the tablet respectively.

#### Friability (F)

Friability of the tablet was determined as specified in official standards using Roche friability test apparatus. A maximum loss of weight (from a single test or from the mean of the three tests) not greater than 1.0 % is acceptable.

#### *In vitro* dissolution studies

All tablet batches were subjected to the dissolution studies using USP II dissolution apparatus. Alkaline Borate buffer (pH 8.4) (900 ml) was used as a dissolution medium kept at a temperature of 37°C and stirred at 50 rpm. The aliquots (5 ml) were withdrawn at

5, 10, 15, 30, 45 and 60 min and replaced with the fresh medium. The samples were analyzed for nimesulide content by UV spectrophotometer at 392nm [20].

## Results and Discussion

Physical properties of starch-silica coprecipitate such as bulk density, tapped density, carr's index and hausner's index were measured and compared with the other available commercial superdisintegrants. Bulk density and tapped density of the starch-silica coprecipitate was found to be 0.75 and 0.88 g/mL respectively. Carr's index and hausner's ratio of the starch-silica coprecipitate were 14.7 and 1.17 respectively indicating excellent flowability characteristics of the starch-silica coprecipitate. The Physical properties of the starch-silica coprecipitate were appreciable in comparison to croscopolvidone and crosscarmellose sodium as depicted in Table 2.

### Scanning Electron Microscopy (SEM)

SEM micrographs of samples showed that the flat irregularly folded sharp edged surface structure of starch (Figure 1) has been transformed into three dimensional structure of starch-silica coprecipitate (Figure 2). The small size of the starch-silica coprecipitate particles suggested that silicon dioxide may have precipitated over the surface of starch. Moreover the coprecipitation of silica onto the surface of starch may result in filling of the folded edges of starch. The finding could be correlated to decrease in surface area of the starch-silica coprecipitate, as reported by Rashid et al.

### FTIR Spectroscopy

The infra red spectrum analysis of starch, silica and starch-silica coprecipitate was performed for studying structural modifications and interaction between the reacting moieties. Starch showed absorption band at 1634 and 2839.39 cm<sup>-1</sup> (Figure 3) and silica showed absorption band at 1119.15 cm<sup>-1</sup> (Figure 4) which is due to Si-O-Si symmetrical stretching vibration. All these bands were identical in the starch-silica coprecipitate (Figure 5). The results suggested the absence of chemical reactivity between starch and silica when they undergo co-precipitation. Moreover both the excipients maintained their independent chemical properties while providing increased functional performance (in terms of superdisintegrant action) after the formation of the starch-silica coprecipitate.

### X-Ray Powder Diffraction

X-ray powder diffraction was performed to monitor the changes in crystallinity characteristics of the product when silica is coprecipitated over starch. Non crystalline materials usually exhibit broad maxima in their XRD spectra. A change in the crystalline characteristics was reported when silica is precipitated over the



**Table 1. Composition used for the preparation of different batches of the fast disintegrating tablets**

| Ingredients                 | B1    | B2    | B3   | B4   | B5    | B6    | B7   | B8   | B9    | B10   | B11  | B12  |
|-----------------------------|-------|-------|------|------|-------|-------|------|------|-------|-------|------|------|
| Nimesulide                  | 50    | 50    | 50   | 50   | 50    | 50    | 50   | 50   | 50    | 50    | 50   | 50   |
| Starch silica coprecipitate | 2.5   | 12.5  | 25   | 50   | ----  | ----  | ---- | ---- | ----  | ----  | ---- | ---- |
| Cross Povidone              | ----  | ----  | ---- | ---- | 2.5   | 12.5  | 25   | 50   | ----  | ----  | ---- | ---- |
| Crosscarmellose sodium      | ----  | ----  | ---- | ---- | ----  | ----  | ---- | ---- | 2.5   | 12.5  | 25   | 50   |
| 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  |
| 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  |
| Avicel                      | 192.5 | 182.5 | 170  | 145  | 192.5 | 182.5 | 170  | 145  | 192.5 | 182.5 | 170  | 145  |

\*all quantities are expressed in mg.

**Table 2. Comparison of physical properties of the starch- silica coprecipitate with other commercial superdisintegrants**

| Physical property | Starch silica co precipitate | Cross povidone       | Cross Carmellose Sodium |
|-------------------|------------------------------|----------------------|-------------------------|
| Bulk density      | 0.75±0.02 g/ml               | 0.54±0.02 g/ml       | 0.67±0.03 g/ml          |
| Tapped density    | 0.88±0.03 g/ml               | 0.67±0.02 g/ml       | 0.74 ±0.02 g/ml         |
| Carr's Index      | 14.70±0.26                   | 20.14±0.05           | 19.50±0.21              |
| Hausner's Ratio   | 1.17±0.05                    | 1.34±0.04            | 1.48 ±0.02              |
| Flowability       | Excellent                    | Fairly passable flow | Fairly passable flow    |

**Table 3. Physicochemical evaluation of the fast dissolving tablets of Nimesulide**

| Formulation | Hardness (Kg/cm <sup>2</sup> ) | Friability (%) | Weight Variation (%) | Disintegrat ion Time (Sec.) | Tensile Strength (T) (MNm <sup>-2</sup> ) | % Drug Release in (5 minutes) |
|-------------|--------------------------------|----------------|----------------------|-----------------------------|---|-------------------------------|
| B1          | 3.5±0.12                       | 0.39           | ±4.2                 | 25±1.2                      | 6.79±0.16                                 | 77.67±1.4                     |
| B2          | 3.7±0.23                       | 0.42           | ±4.1                 | 24±1.1                      | 7.75±0.05                                 | 78.66±1.6                     |
| B3          | 3.2±0.64                       | 0.45           | ±4.5                 | 25±1.5                      | 5.92±0.03                                 | 79.33±1.6                     |
| B4          | 3.4±0.27                       | 0.52           | ±4.8                 | 26±1.7                      | 6.60±0.03                                 | 78.61±1.5                     |
| B5          | 3.1±0.56                       | 0.48           | ±4.3                 | 75±1.3                      | 5.36±0.01                                 | 37.65±1.1                     |
| B6          | 3.5±0.43                       | 0.45           | ±4.7                 | 63±1.2                      | 5.80±0.02                                 | 54.18±1.3                     |
| B7          | 3.6±0.29                       | 0.46           | ±4.4                 | 54±2.1                      | 6.23±0.02                                 | 66.12±2.2                     |
| B8          | 3.2±0.48                       | 0.38           | ±4.6                 | 78±2.1                      | 5.19±0.01                                 | 60.97±2.1                     |
| B9          | 3.8±0.39                       | 0.55           | ±4.1                 | 69±1.8                      | 7.20±0.04                                 | 51.79±1.9                     |
| B10         | 3.6±0.19                       | 0.42           | ±4.4                 | 58±2.2                      | 6.66±0.05                                 | 67.40±2.0                     |
| B11         | 3.3±0.27                       | 0.56           | ±4.2                 | 52 ±1.7                     | 5.97±0.03                                 | 72.73±2.1                     |
| B12         | 3.7±0.53                       | 0.53           | ±4.1                 | 70±2.3                      | 7.18±0.03                                 | 48.67±1.4                     |

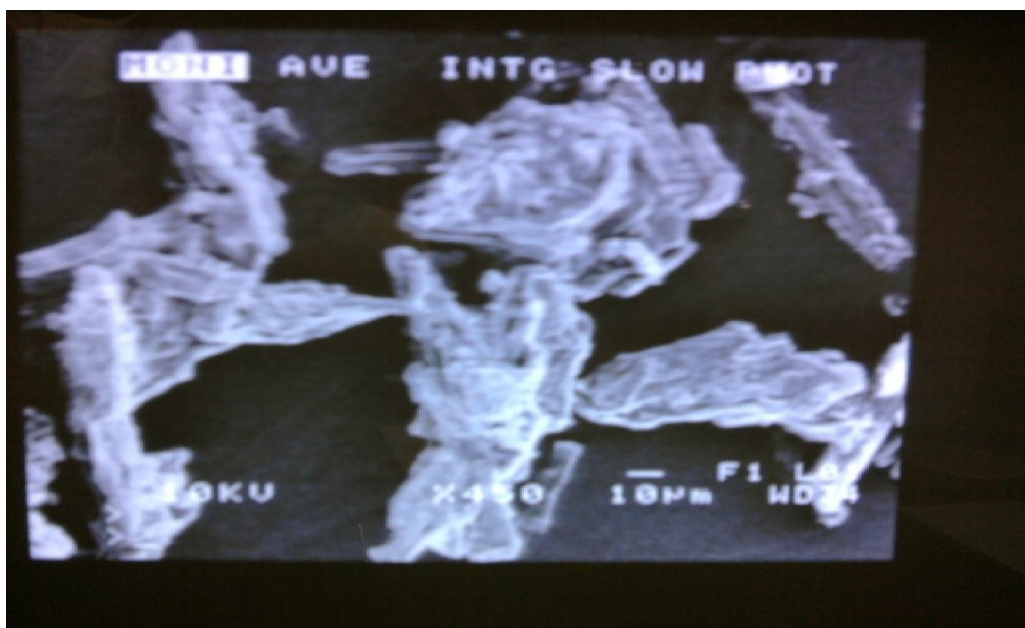


Figure 1. Scanning Electron Micrograph of starch



Figure 2. Scanning Electron Micrograph of Starch-Silica coprecipitate



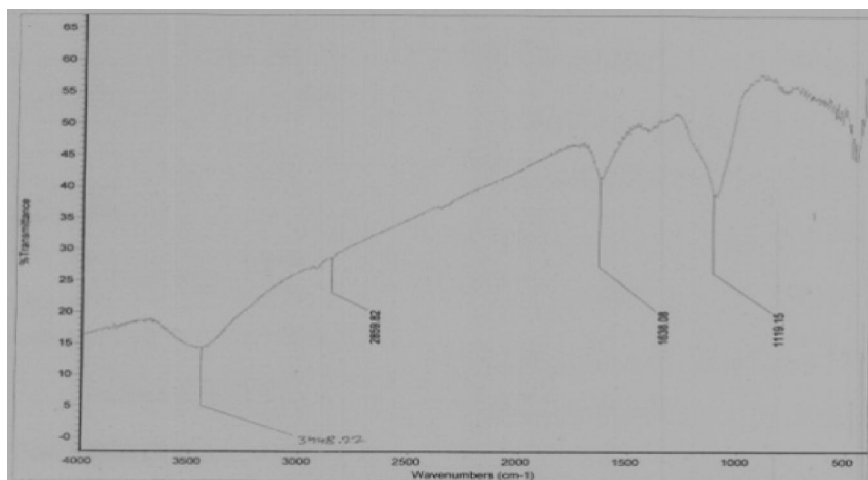


Figure 3. FTIR spectrum of starch

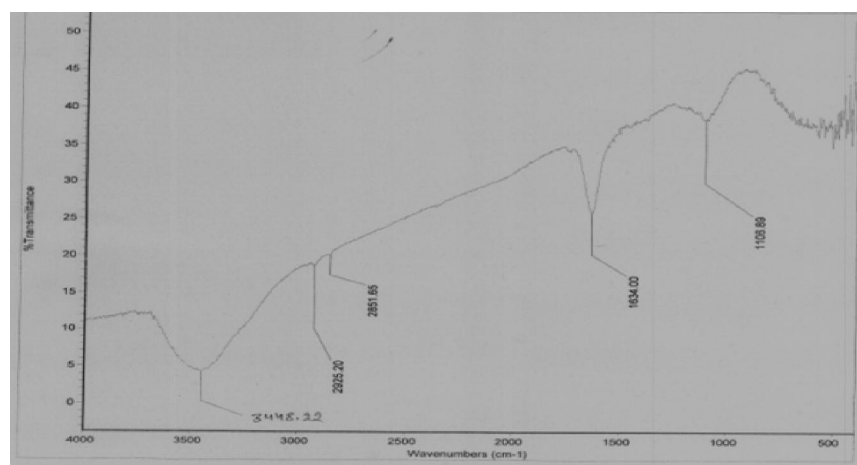


Figure 4. FTIR spectrum of silicon dioxide

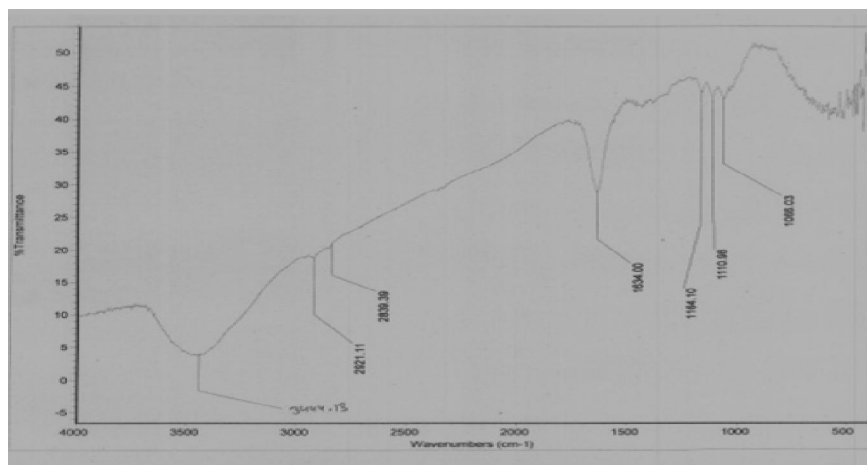


Figure 5. FTIR spectrum of starch-silica coprecipitate



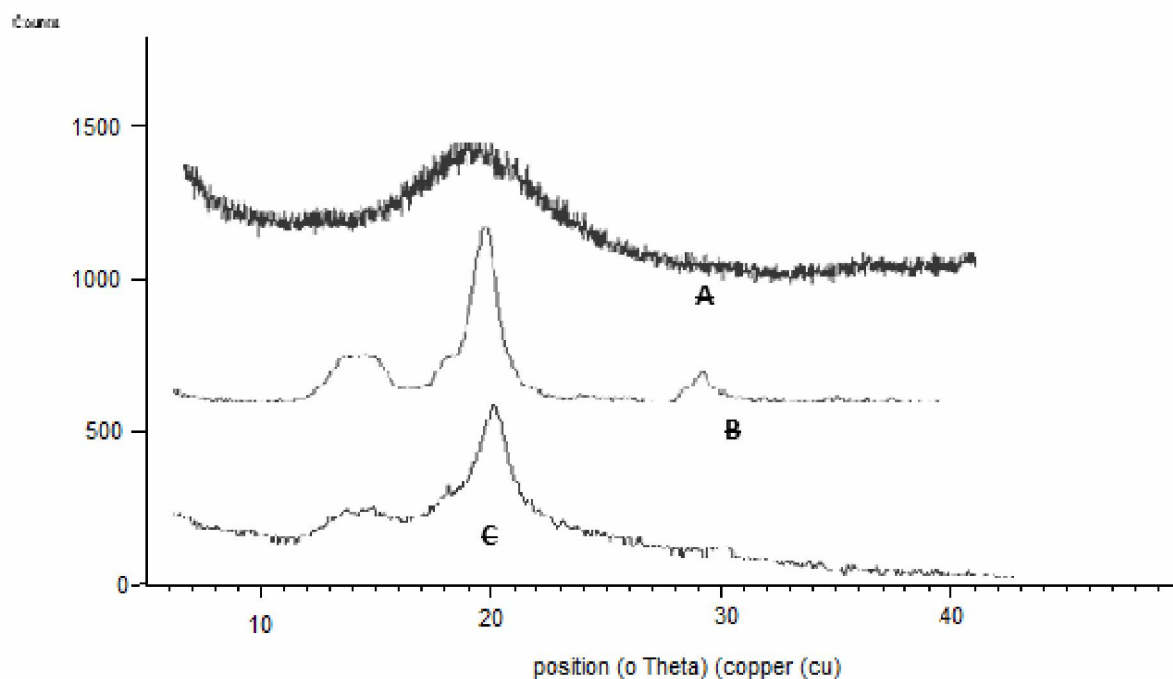


Figure 6. Overlay XRD spectrum of A. Silicon Dioxide B. Starch C. Starch-Silica coprecipitate

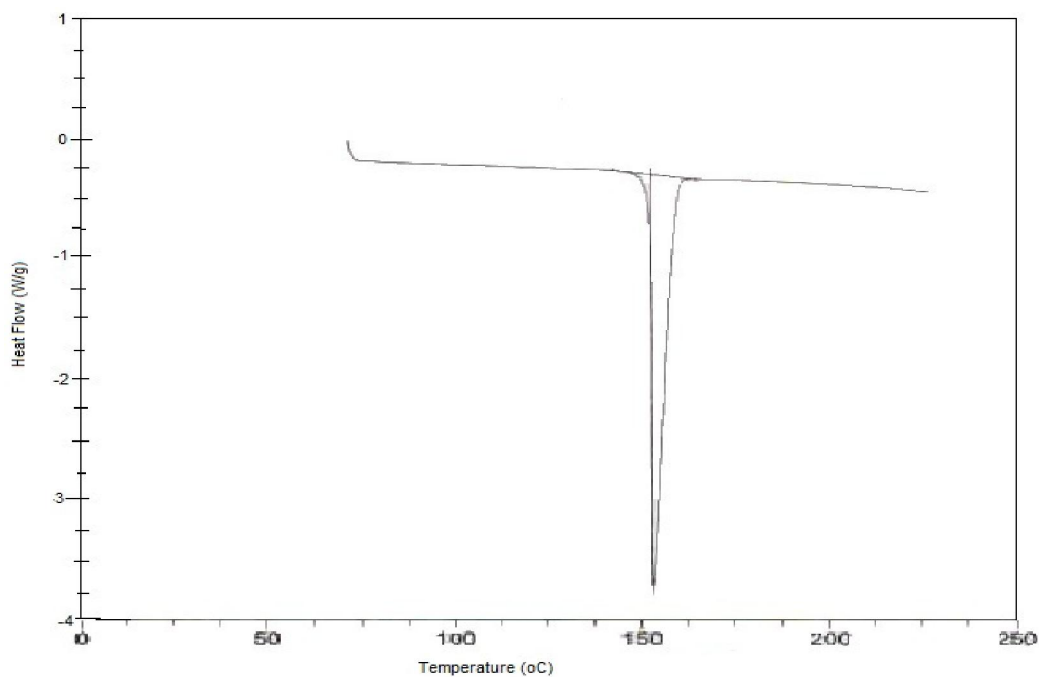


Figure 7. DSC thermogram of pure drug nimesulide



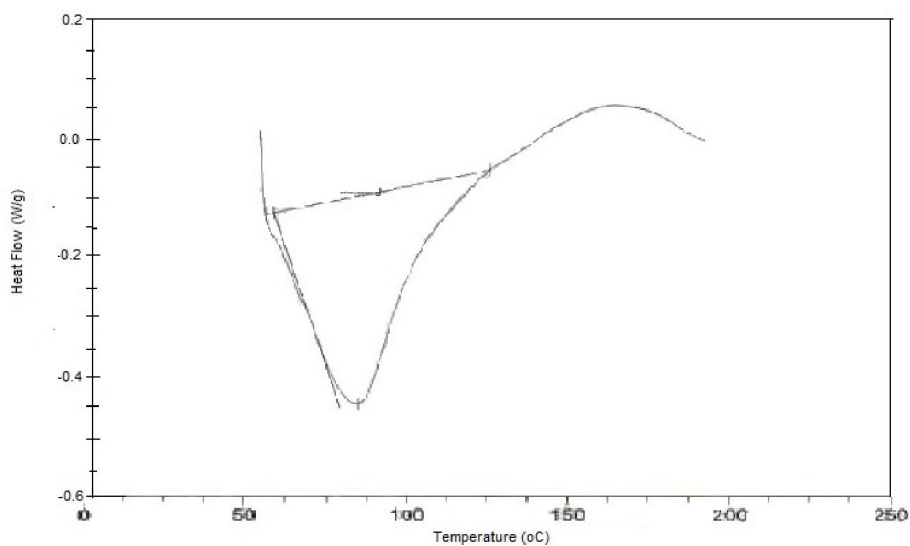


Figure 8. DSC thermogram of starch-silica coprecipitate

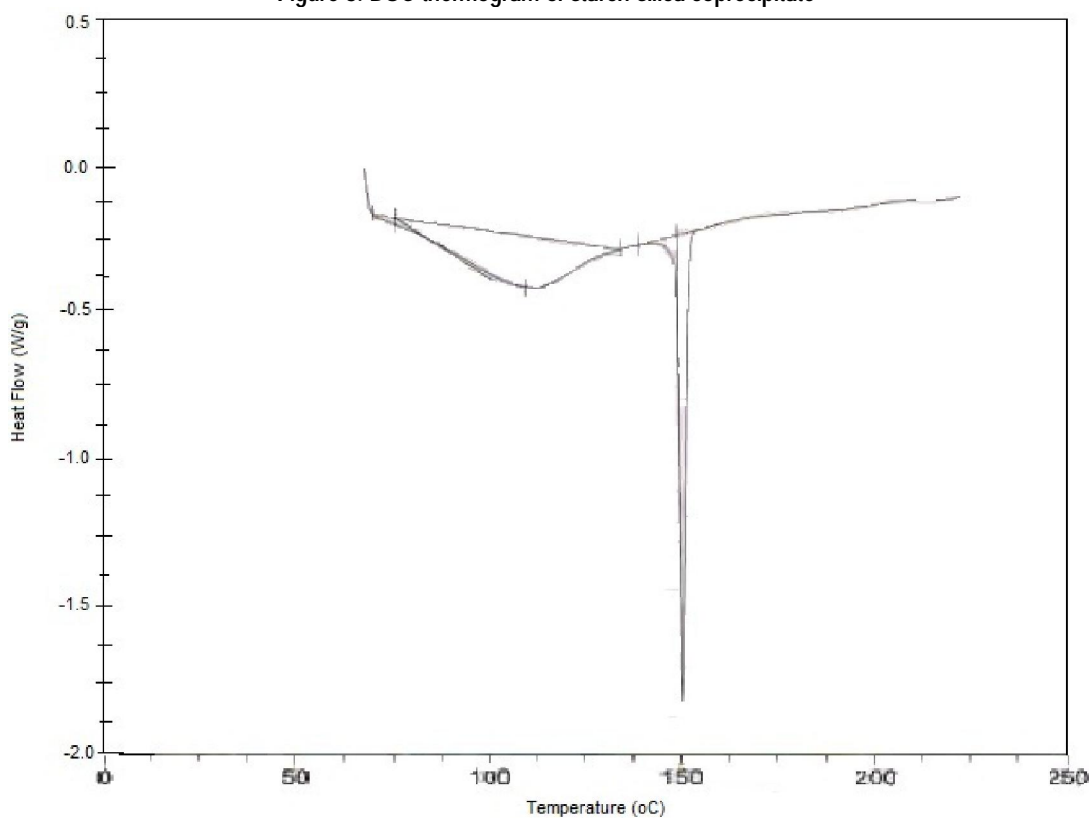


Figure 9. DSC thermogram of physical mixture of drug and coprecipitate in 1:1





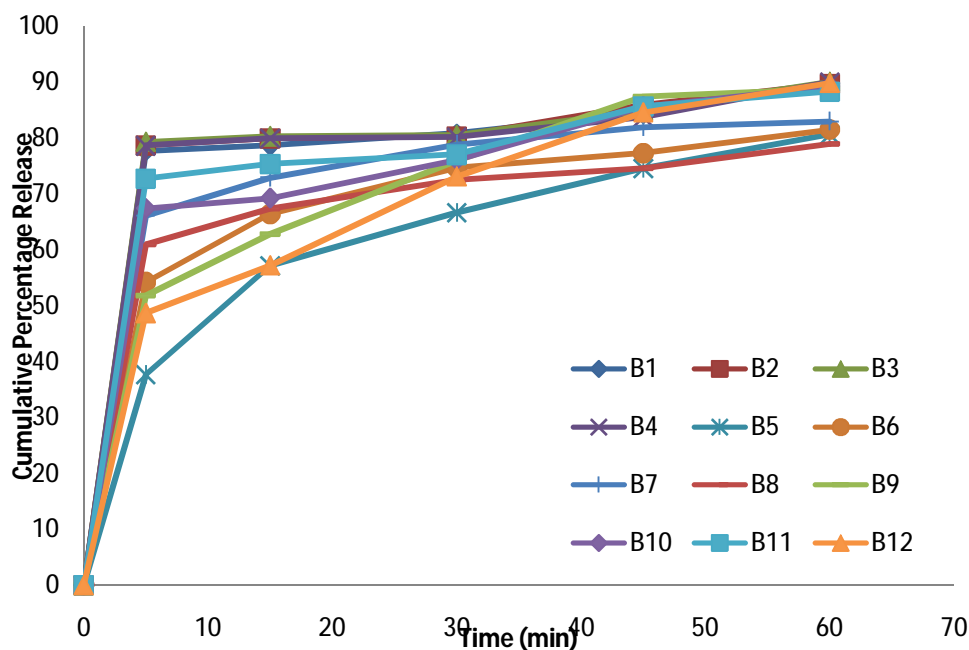


Figure 10. *In vitro* dissolution Profile of all formulations batches (B1-B12)

starch. Figure 6 shows the diffraction patterns of starch, silica and starch-silica coprecipitate. The amorphous form of the starch established partial crystalline characteristics on precipitation of the silica over the starch. Starch showed three broad peaks at 20.3, 22.5 and 34.4 having peak areas 167.89, 379.89 and 62.91 respectively, which may be due to the distributed crystal structure of the starch. XRD spectra of silica exhibited the presence of broad peak at 26.28. Appearance of two sharp and narrow peaks at 22.6 and 34.3 with peak area 114.07 and 18.14 respectively in the XRD spectra of starch silica co precipitate point out towards the reduction of powder's amorphous region and appearance of the crystalline characteristics.

### Differential scanning calorimetry

Differential scanning calorimetry (DSC) is a technique for measuring the physical transformation of the drugs when they undergo phase transitions due to endothermic or exothermic heat flows. Nimesulide showed an endothermic heat flow at 152.5 °C corresponding to melting with decomposition (Figure 7). Starch-silica coprecipitate showed decomposition endothermic heat flow at a temperature range of 147.23 - 153.26 °C (Figure 8). No shift in the decomposition temperature range of starch-silica coprecipitate and nimesulide endothermic peak when starch-silica coprecipitate was mixed with nimesulide at the mass ratio of 1:1, as observed by DSC thermogram (Figure 9). This indicates the chemical compatibility of nimesulide with starch-silica and hence the absence of any new chemical entities.

### Physicochemical evaluation of tablets

Tablets prepared with the starch-silica coprecipitate showed better disintegration characteristics as compared to tablets prepared using crosspovidone and crosscarmellose sodium (Table 3). DT value of less than 30 sec was observed at low concentration (1%) of the starch silica co precipitate whereas DT of more than 50 sec was observed with CCS and CP at higher concentrations (10%), suggesting better superdisintegrant action of coprecipitate over conventional superdisintegrants. Moreover, the DT was independent of concentration of coprecipitate (almost same at all concentrations) whereas in case of crosscarmellose sodium and crosspovidone, the DT value decreases with increase in concentration upto 10%, after that (at 20%) it increases. Hardness of all tablet batches was found to be almost same. All tablet batches passed the friability (% weight loss is < 1%) and weight variation test. The tensile strength was found to ranged from 5.92 to 7.752 (B1 to B4), 5.199 to 6.230 (B5 to B8) and 5.971 to 7.203 (B9 to B12) (Table 3).

### *In vitro* drug release

*In vitro* dissolution profiles of prepared batches of FDTs using crosscarmellose sodium, crosspovidone and starch silica coprecipitate as superdisintegrants are depicted in Figure 10. Tablet containing starch-silica coprecipitate (batch B1-B4) exhibited > 70% release after 5 min at all concentrations (1-20%) whereas tablets containing CP and CCS as superdisintegrant (batch B5-B8, B9-B12 respectively) showed > 60% release at a

concentration of 10% indicating better disintegration and drug release characteristics caused by the coprecipitate over existing superdisintegrants.

## Conclusion

In summary, starch-silica coprecipitate showed the improved characteristics as superdisintegrants as compared to the conventional superdisintegrants. The coprecipitate act as inert material with better compressibility characteristics over conventional superdisintegrants. Moreover no interaction with the drug particles as confirmed by DSC studies suggested that it can be used as an excipient in tablet dosage form. Better disintegration characteristics exhibited by coprecipitate over conventional superdisintegrants suggested that it can be commercially exploited for industrial purpose.

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## Author's Contributions

MN and IBS participated in the design of the study and drafted the manuscript. AG and SK carried out all the experimental studies. All authors read and approved the final manuscript.

## Conflict of Interest

There is no conflict of interest

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