ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Formulation and Evaluation of Orally Disintegrating Tablet of Niacinamide

Reeta Rani Thakur[1], Sonia Narwal[1]

[1]Dept of Pharmaceutics, MM College of Pharmacy, MM University, Mullana, Ambala (india)

ABSTRACT

The aim of present investigation was formulation and evaluation of orally disintegrating tablets of Niacinamide. Orally disintegrating tablets offers a solution for Pediatrics, geriatrics; psychiatrics or mentally ill peoples and those who have difficulty in swallowing tablets/capsules resulting in improved patient compliance. Orally disintegrating tablets of Niacinamide were prepared with the addition of different superdisintegrants namely crospovidone,Croscamellose sodium and sodium starch glycolate.Each of these superdisintegrants were used in the conc. of 3-7%w/w,3-5%w/w and 3-5%w/w.Mannitol is used as a filler. Nine formulations having different superdisintegrants at different concentration levels were prepared to assess their efficiency and critical concentration level. The tablets were evaluated for hardness, friability, weight variation, disintegration time, diameter, thickness and wetting time, in vitro dissolution studies and friability. The hardness of the tablets was in the range of 3.26 - 4.19Kg/cm². All the formulations shows disintegration time in the range of 36-58 sec.The percentage friability of the tablets was less than one. It was found that Formulation S1, S2 and S3 which contains increase conc. of Sodium starch glycolate from 3%-5% w/w have recorded drug release 99.84%, 97.25% and 96.44%. Maximum drug release was observed with sodium starch glycolte excipient prepared by direct compression method.

Keywords: Crospovidone, Cros**c**armellose Sodium, Sodium Starch Glycolate, ODT, Niacianmide, Superdisintegrants.

Corresponding author

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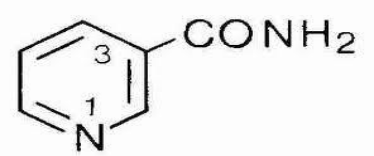
INTRODUCTION

The centre for drug evaluation and Research defines orally disintegrating tablets as a dosage form –"A solid dosage form which disintegrates rapidly within a matter of seconds when placed under the tongue". The disintegrating time for orally disintegrating tablet varies from seconds to minutes, depends upon the size of tablet and formulation. European pharmacopeia defined orally disintegrating tablets as-"Uncovered tablet which disperse before ingestion in the buccal cavity" [2]. Different technological techniques such as freeze drying, Spray drying, Sublimation, direct compression etc.are used to prepare the formulation of this type in the pharmaceutical market .Direct compression is one of the technique. It requires the incorporation of superdisintegrants into the formulation to achieve fast disintegration of tablets. Direct compression does not require the use of water or heat during the formulation procedure. It is the ideal method for moisture and heat-labile medicaments. They are also suitable for the mentally ill, the bed-ridden, and patients who do not have easy access to water. The benefits, in terms of patient compliance, rapid onset of action, increased bioavailability, and good stability make these tablets popular as a dosage form of choice in the current market. Orally disintegrating tablets are also called as Fast dissolving tablets, mouth-dissolving tablets, melt-in mouth tablets, Orodispersible tablets, rap melts, porous tablets, quick dissolving etc [3].

Niacinamide (Pyridine-3-Carboxamide) is a Biopharmaceutical Classification System I drug based on its high solubility in water and good permeability. Its melting point is in the range of 128-131ºC.It's Elimination half-life is 20-45 mins. It is colorless crystal or a white crystalline powder, dour faint and characteristics. It contains not less than 99.0 percent and not more than 101.0 percent of $C_6H_6N_20$, calculated on the dried basis (I.P., B.P.).It is freely soluble in water and in ethanol.



It is used for treating diabetes and two skin conditions called Pemphigoid and granuloma annulare.It is also used for acne, leprosy, memory loss, arthritis, preventing premenstrual headache, improves digestion, lowering blood pressure and prevent cataracts. It is used for preventing vt-B_3 deficiency, pellagra, schizophrenia, hallucination due to drug.Furthermore, Niacinamide is administered by oral and intramuscular routes and its molecular formula is $C_6H_6N_20$.Niacinamide is possibly safe when used appropriately in childrens.It also prevents immunosupression caused by UVA and UVB radiations.

MATERIALS AND METHOD

Niacinamide was purchased from Kukreja Pharma. Sodium starch Glycolate (SSG), Crosspovidone, Crosscarmellose Sodium, Mannitol, Talc, Magnesium stearate, Microcrystallian cellulose and Aspartame were gifted by Apcer Pharma. All other ingredients used were of analytical grade.

ISSN: 0975-8585

FOURIER TRANSFORM INFRARED SPECTROSCOPY (FTIR)

The study was carried out to determine the molecular structure serving as an identification test to ascertain the purity of molecule.IR spectroscopy was obtained by FTIR spectrophotometer (Shimadzu) made in Japan using NaCl pellets. The spectrum was recorded for pure drug. The scanning range used was 400-4000 cm^{-1} and the resolution was 1 cm^{-1}

COMPATIBILITY STUDIES

Powder X-ray diffraction patterns were recorded using x-ray diffractometer to check the compatibility between Drug and disintegrants. under the following conditions : target C4 , Filter Ni , voltage 45kv, current 40 mA receiving slit 91mm. the data were collected in continues scan mode using stepwise of 0.10C at 2 / sec. the scanned range was 10 - 40ºC.

PREPARATION OF TEST TABLETS

Niacinamide orally disintegrating tablets were prepared by direct compression method. Different concentration of excipients was used to prepare different groups of orally disintegrating tablets. Compositions of various formulations are shown in Table 1. All ingredients first pass through sieve no. 80. All the ingredients without magnesium stearate and talc were mixed uniformly followed by addition of magnesium stearate and talc. The prepared powder blend was evaluated for various parameters like bulk density, tapped density, angle of repose, compressibility index and Hausner ratio. After evaluation of powder blend the tablets were compressed with single station tablet punching machine. The total weight of the formulation was maintained 250mg.

Table1: Composition of Ingredients used in Selected Formula

Ingredients(mg/tab)	CP1	CP2	CP3	CM1	CM2	CM3	S1	S2	S3
Drug	100	100	100	100	100	100	100	100	100
Croscarmellose	0	0	0	7.5	10	12.5	0	0	0
sodium									
Crospovidone	7.5	10	12.5	0	0	0	0	0	0
Sodium starch	0	0	0	0	0	0	7.5	10	12.5
Glycolate									
Aspartame	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Magnesium	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
stearate									
Talc	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Microcrystalline	50	50	50	50	50	50	50	50	50
cellulose									
Mannitol(q.s.)	85	82.5	80	85	82.5	80	85	82.5	80

ISSN: 0975-8585

X-RAY DIFFRACTION STUDY

The powder XRD pattern of pure drug (Fig-1) and with the excipients crospovidone (Fig-2), croscarmellose sodium (Fig-3) and sodium starch glycolate (Fig-4) showed that drug was highly crystalline in nature as indicated by the distinctive peaks. The degree of crystallinity of pure drug does not change in its mixture form. The peak intensity however decreased due to lesser fraction of pure drug in its mixture form with excipients.

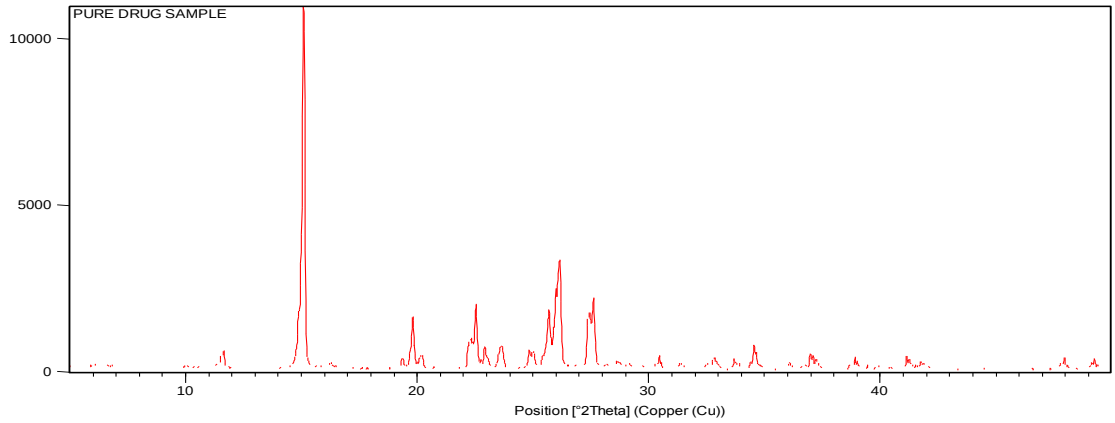


Fig. 1: XRD pattern of pure Niacinamide

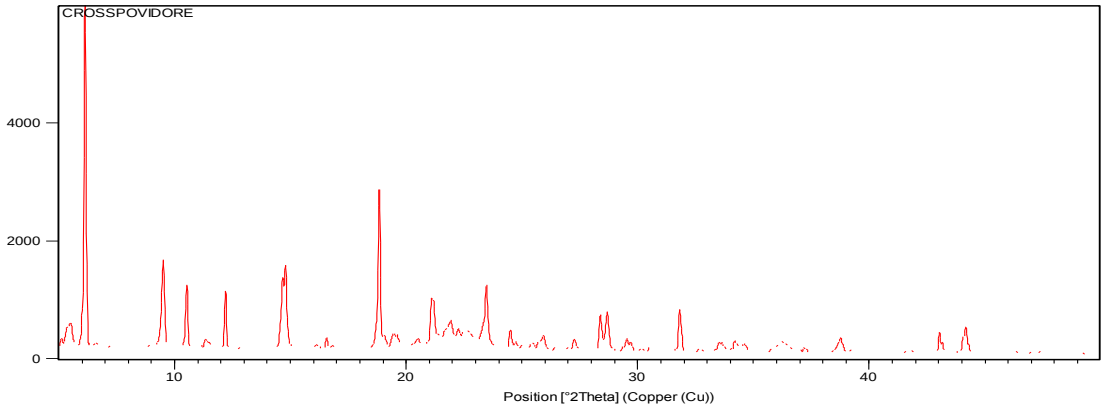


Fig. 2: XRD pattern of pure Niacinamide and Crosspovidone

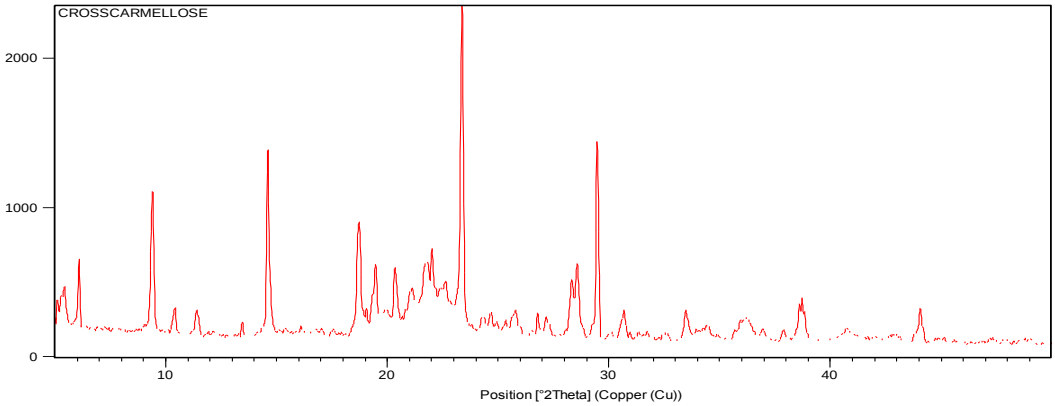


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Fig. 3: XRD pattern of pure Niacinamide and Croscarmellose sodium

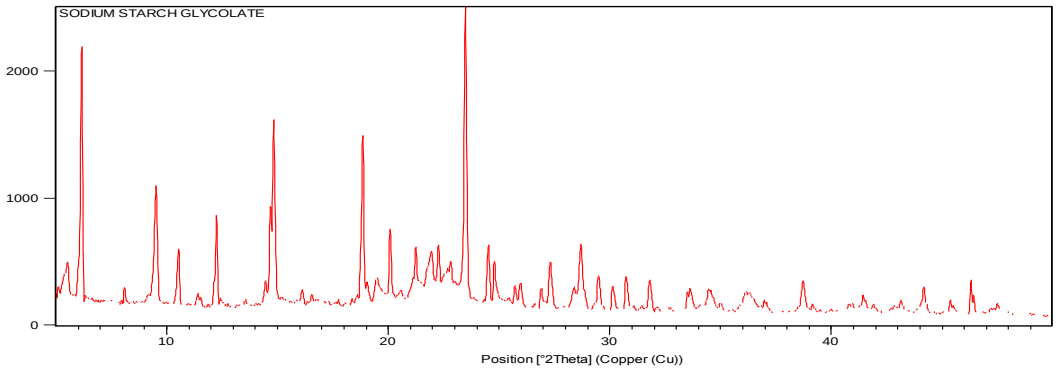

Fig. 4: XRD pattern of pure Niacinamide and Sodium starch glycolate

CHARACTERIZATION OF ORALLY DISINTEGRATING TABLETS:

Evaluation of powder blend [1, 5, 7, 8]

Angle of Repose

Angle of repose (α) was determined using funnel method. The blend was poured through a funnel that can be raised vertically until a maximum cone height (*h*) was obtained. The radius of the heap (*r*) was measured and angle of repose was calculated.

$$A = \tan^{-1}(h/r)$$

Bulk Density (ρb)

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weighed powder into a measuring cylinder and initial weight was noted. This initial volume was called the bulk volume. From this the bulk density was calculated according to the formula mentioned below. It is expressed in gm/ml.

$$\rho b = M/Vb$$

Where, M and Vb are mass of powder and bulk volume of the powder respectively.

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Tapped Density (ρt)

The measuring cylinder containing a known mass of blend was tapped for a fixed time. The minimum volume (vt) occupied in the cylinder and the weight (m) of the blend was measured. The tapped density was calculated using the following formula,

$$\rho t = M/Vt$$

Carr's compressibility index

The simplest way of measurement of free flow of powder is compressibility, an indication of the ease with which a material can be induced to flow is given by compressibility. The compressibility index of the granules was determined by Carr's compressibility index which is calculated by using the following formula

$$C = (V_0 - V_t / V_0) \times 100$$

Hausner ratio

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

$$\text{Hausner ratio} = \rho t / \rho b$$

Where ρt is tapped density and ρb is bulk density.

Table II: Pre-compression characteristics of powder blend

Parameters	CP1	CP2	CP3	CM1	CM2	CM3	S1	S2	S3
Angle of Repose	26.23±0.02	24.02±0.03	23.22±0.03	26.62±0.01	23.98±0.02	25.81±0.04	24.69±0.02	23.17±0.03	24.97±0.4
Bulk density (kg/cm^3)	0.458±0.03	0.592±0.01	0.683±0.03	0.561±0.07	0.464±0.05	0.612±0.05	0.639±0.05	0.511±0.04	0.594±0.02
Tapped Density (kg/cm^3)	0.529±0.07	0.652±0.01	0.667±0.08	0.539±0.03	0.610±0.03	0.799±0.02	0.715±0.05	0.510±0.04	0.639±0.01
Carr´s Index (%)	10.42	12.5	10.95	11.27	10.99	10.89	11.6	10.76	11.1
Hausner´s Ratio	1.15±0.05	1.17±0.02	1.12±0.02	1.11±0.04	1.17±0.02	1.16±0.08	1.13±0.04	1.12±0.05	1.14±0.09

EVALUATION OF ORALLY DISINTEGRATING TABLETS OF NIACINAMIDE

All the batches of tablets were evaluated for various parameters like Weight variation, Friability, Hardness,Thickness,Diameter,In-vitro disintegration time, Disintegration time, Wetting time and Dissolution and results reported in Table 3.

Weight variation Test

Twenty tablets were taken and their weight was determined individually and collectively on a digital weighting balance. The average weight of one tablet was determined from the collective weight [4, 5].

Hardness Test

The resistance of tablets to shipping or breakage under the conditions of storage, transportations and handling before usage depends on its hardness. The hardness of tablet was measured by Monsanto hardness tester. The hardness was measured in terms of Kg/cm². [6].

Thickness and Diameter

Thickness and diameter of tablets were determined using vernier caliper. Five tablets from each batch were used, and an average value was calculated. It was measured in mm. [12]

In-vitro dispersion time

To determine dispersion time 10 ml measuring cylinder was taken in which 6 ml distilled water was added and tablet was dropped in it. Time required for complete dispersion was determined. [3, 6]

Disintegration time

The test was carried out on 6 tablets using the apparatus specified in I.P.-1996 distilled water at $37^{o}C \pm 2^{o}C$ was used as a disintegration media and the time in second taken for complete disintegration of the tablet with no palatable mass remaining in the apparatus was measured in seconds [10,12].

Wetting time

Five circular tissue papers of 10 cm diameter are placed in a petridish with a 10 cm diameter [9]. Ten millimeters of water-containing Amaranth, a water-soluble dye, is added to petridish. A tablet is carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet is noted as a wetting time. It was measured in seconds.

Friability Test [11]

Friability of the tablets was determined using Roche friability (Electrolab). This device subjects the tablets to the combined effect of abrasions and shock in a plastic Chamber revolving at 25 rpm and dropping the tablets at a height of 6 inches in each revolution. Preweighed sample of tablets was placed in the friabilator and were subjected to 100

ISSN: 0975-8585

revolutions. Tablets were de dusted using a soft muslin cloth and reweighed. The friability (f) is given by the formula.

$$f = (1- W0 / W) \times 100$$

Where, W0 is weight of the tablets before the test and W is the weight of the tablet after test.

Table III: Post-compression evaluation of prepared tablets

Parameters	CP1	CP2	CP3	CM1	CM2	CM3	S1	S2	S3
Hardness(Kg/cm^2)	4.19	3.45	3.82	3.96	4.15	3.87	3.26	3.54	3.65
Thickness(mm)	4.5	4.39	4.42	4.85	4.54	4.5	4.48	4.3	4.59
Diameter(mm)	9.1	8.75	8.92	9.2	9.45	8.64	8.98	9.3	9.76
Wetting time(sec)	42	54	45	68	49	61	57	54	49
Wt.variation(mg)	249	251	247	253	249	253	250	248.8	252
Friability (%)	0.893	0.531	0.687	0.85	0.586	0.768	0.653	0.541	0.719
Disinte.time(sec)	36	58	42	45	57	53	39	55	48
Dispers.time(sec)	42	36	58	54	49	39.6	40	60	54

IN -VITRO DISSOLUTION

In vitro dissolution studies of Niacinamide formulated tablets were studied using USP dissolution Apparatus II. Simulated Saliva was taken as dissolution medium, the volume being 900 mL. The temperature was maintained at 37 ± 0.5C^0. The rotation speed was 50 rpm. Five milliliters of aliquot were withdrawn at predetermined time of intervals. The medium was refilled with 5 mL of Simulated Saliva each time. Sample was analyzed by using UV at 261nm. The study was performed in triplicate.[2, 5]

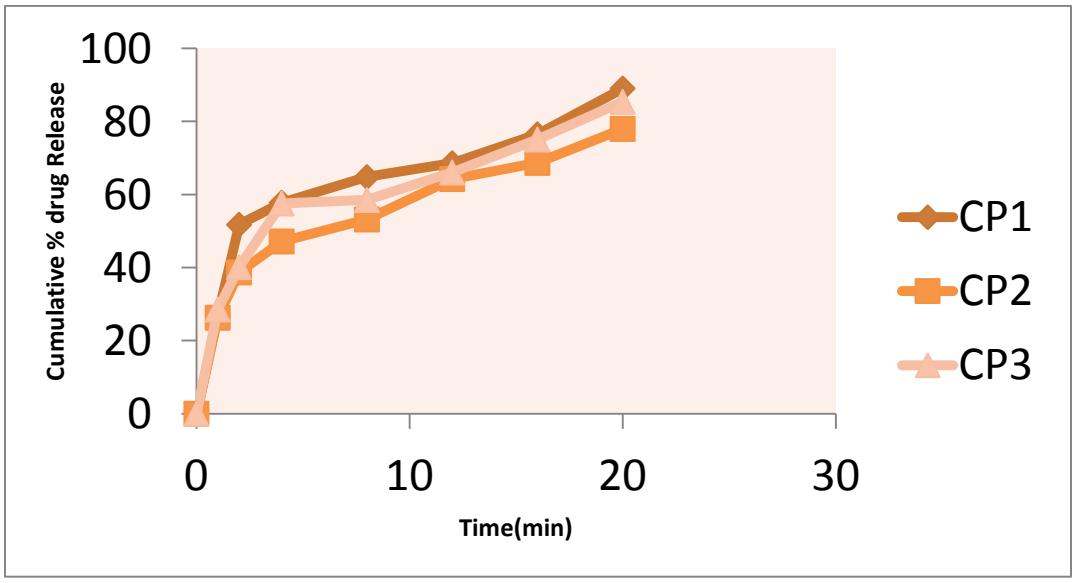

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Fig. 5: Graphical representation of comparative dissolution study of formulation of Niacinamide prepared by Crospovidone

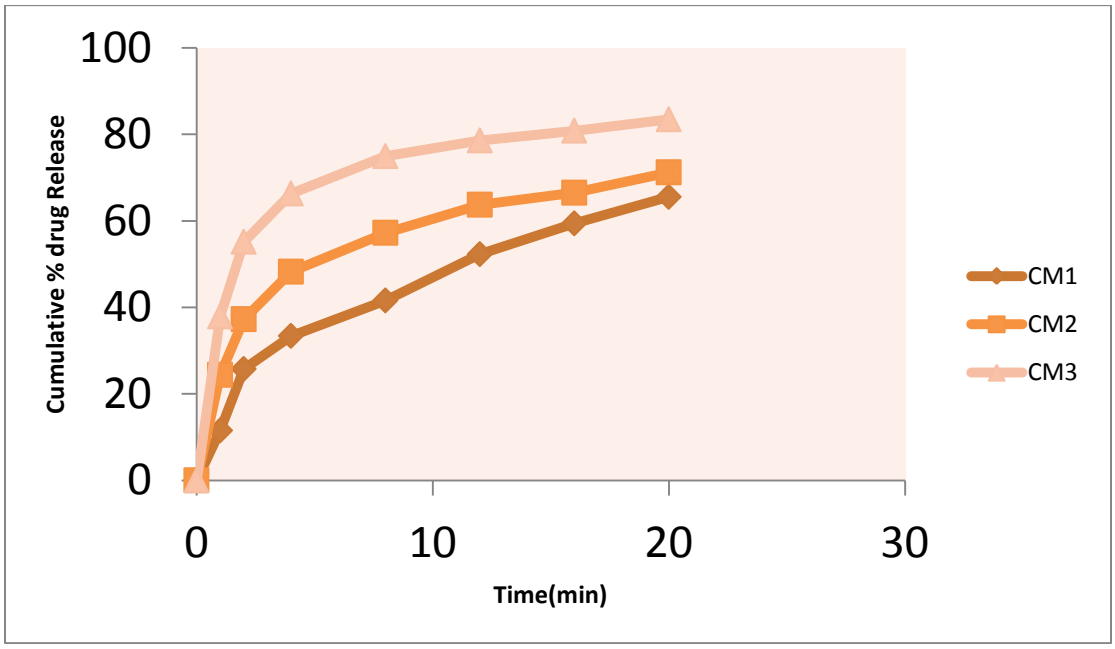

Fig. 6: Graphical representation of comparative dissolution study of formulation of Niacinamide prepared by Croscarmellose sodium

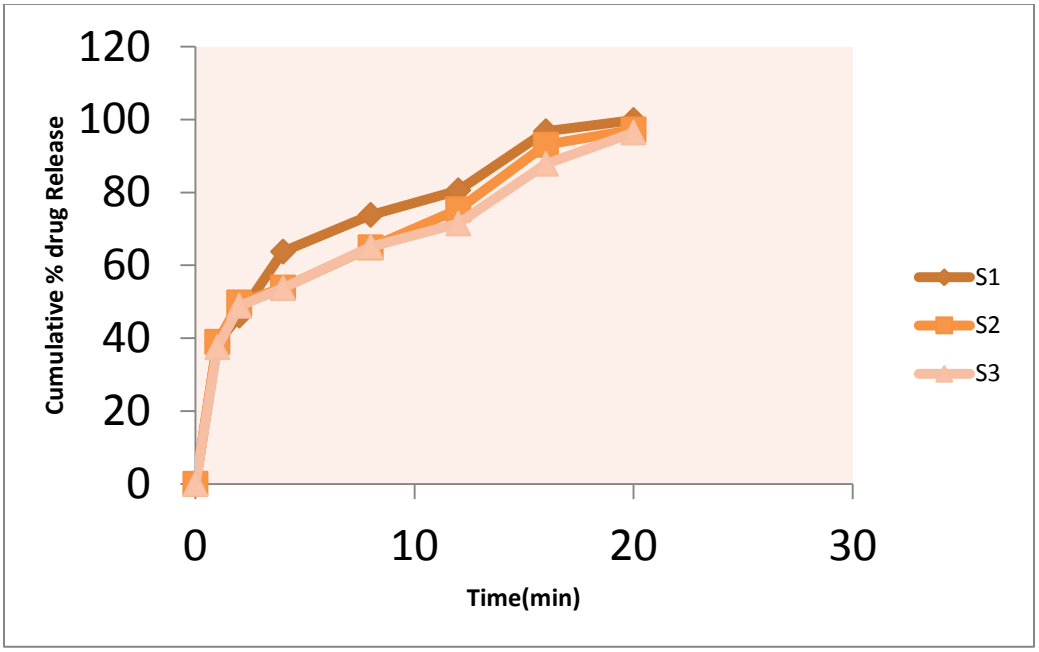

Fig. 7: Graphical representation of comparative dissolution study of formulation of Niacinamide prepared by Sodium starch glycolate

ISSN: 0975-8585

RESULT AND DISCUSSION

Niacinamide orally disintegrating tablets were prepared by direct compression method. Three different groups (CP, CM, and SSG) of formulation with different conc. of superdisintegrant were prepared with each group containing three different formulations. Table 3 shows the data obtained from the evaluation of tablets. All batches of the tablets were evaluated for various physical parameters such as hardness, thickness, diameter, friability, wetting time, disintegration time, In-vitro dispersion time, weight variation and In-vitro dissolution which was reported in Table no 3. All above properties and value were near to boundary of standard limit. All the tablets maintained hardness in the range 3.26–4.19kg/cm^2. The loss in total weight of the tablets due to friability was in the range of 0.53-0.89%. The thickness in different formulation was highly uniform and in the range of 4.3-4.85mm.The diameter of different formulations was in the range of 8.64-9.76mm. Wetting time is used as an indicator of the ease of tablet disintegration and found to be 42-68sec. Weight variation ranged from 247.8-253.8mg The result in vitro dispersion time were within the prescribe limit and comply with the criteria for orally disintegrating tablets, the value were with 36-60 sec. In vitro dissolution studies are shown in fig.5, 6 and 7. Formulation CP1, CP2 and CP3 which contains increase conc. of Crospovidone from 3%-5% w/w have recorded drug release 89.06%,77.98% and 85.4%,formulation CM1, CM2 and CM3 which contains increase conc. of Croscarmellose sodium from 3%-5% w/w have recorded drug release 65.54%,71.22% and 83.49% and formulation S1,S2 and S3 which contains increase conc. of Sodium starch glycolate from 3%-5% w/w have recorded drug release 99.84%,97.25% and 96.44%.

CONCLUSION

In the present study it can be concluded from the characterization of orally disintegrating tablets of Niacinamide that formulation containing Sodium Starch Glycolate is most acceptable because On comparing the formulation of Crosspovidone, Croscarmellose Sodium and Sodium Starch Glycolate among themselves, CP1, CM3 and S1was found best respectively and on comparing these three formulations it was found that SI was the best because it release 99% drug.

ACKNOWLEDGEMENT

I would like to acknowledge Department of Pharmacy, M. M. University for providing the facilities for research work.

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