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FORMULATION AND DEVELOPMENT OF DISINTEGRATING TABLET FOR ORAL REHYDRATION THERAPY (ORT) FOR ZINC SULPHATE

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ABSTRACT

Zinc supplementation plays a critical role in reducing the duration and severity of acute diarrhea, particularly in pediatric patients. However, conventional zinc sulphate tablets often suffer from poor palatability and low patient compliance, especially among children. The present study aims to formulate and evaluate mouth disintegrating tablets (MDTs) of Zinc Sulphate, designed to enhance ease of administration, improve patient compliance, and deliver rapid therapeutic action as part of Oral Rehydration Therapy (ORT). Five formulations (F1–F5) were developed using direct compression technique, incorporating Zinc Sulphate Monohydrate (equivalent to 20 mg elemental zinc) along with suitable excipients. Superdisintegrants were varied across formulations to assess their impact on disintegration and drug release. Angle of repose, bulk/tapped density, compressibility index, and other pre-compression characteristics were assessed for each batch. Post-compression measurements included in-vitro dissolution, drug content uniformity, weight variation, disintegration time, tablet hardness, and friability. With a disintegration time of less than 30 seconds, a drug content of 99.2%, and a drug release of more than 99% within 15 minutes, Formulation F5 was the finest of all. FTIR studies revealed no drug–excipient interaction, despite stability tests over three months in accelerated conditions (40 ± 2 °C / 75 ± 5% RH) showing the formulation remained stable in terms of appearance, drug content, and release profile.

KEYWORDS: Zinc sulphate, Oral rehydration therapy, Mouth disintegrating tablet.

INTRODUCTION

Oral Rehydration Therapy (ORT) is a globally recognized method for treating dehydration caused by diarrhea, vomiting, or excessive fluid loss. The development of disintegrating tablets for ORT aims to enhance the rapid rehydration process by improving the dissolution and absorption of electrolytes. This innovative approach seeks to address the limitations of conventional oral rehydration salts (ORS), such as delayed dissolution and the need for water for preparation, ensuring immediate therapeutic action. **(Sager et al., 2011).** One of the most important treatments for dehydration brought on by vomiting, diarrhoea, or other conditions that induce fluid and electrolyte loss is oral rehydration therapy, or ORT. It is recommended by the World Health Organisation (WHO) and UNICEF as a safe, economical, and effective way to relieve dehydration, especially in environments with limited resources. Traditional oral rehydration salts (ORS) solutions require mixing with water, which can limit their use due to the need for clean water, proper storage, and preparation methods. To address these challenges, the formulation of an orally disintegrating tablet (ODT) for ORT, incorporating super disintegrants, has been proposed. ODTs dissolve rapidly in the oral cavity without the need for water, ensuring rapid absorption and ease of administration, particularly in pediatric, geriatric, and emergency settings. This synopsis explores the formulation, development, and evaluation of super disintegrant-based ODTs for effective ORT. Patients who are elderly, paediatric, bedridden, or have developmental disabilities are the main target audience for these novel mouth-dispersing dose formulations. FDDTs are also an excellent option for patients who have chronic nausea, are travelling, or have limited or no access to water. Other patient populations will soon be the focus as well. FDDTs have a new use in veterinary medicine, such as preventing cats from being pilled. Fast-dissolving/disintegration tablets' pleasant flavour and convenience of administration may motivate patients to take their medications on a daily basis. Nandhini M. et al. (2024) conducted a study The effects of the natural super disintegrating ingredients in the Dapsone fast-dissolving tablets were compared. The natural super disintegrating agents were characterised using a number of physicochemical approaches, including moisture content, ash values, and loss on drying. In 2024, Zieg J. and others Volume depletion is a common problem that commonly results in hospitalisation for children. A competent medical assessment must include both a thorough history and a thorough physical examination. In some cases, biochemical testing may be useful. In order to treat fluid balance properly, it is necessary to comprehend its pathophysiology.

The effects of the Dapsone fast-dissolving pills' natural super disintegrating chemicals were contrasted. Moisture content, ash values, and drying loss were among the physicochemical methods used to characterise the natural super disintegrating agents. Zieg J. and others in 2024 Volume depletion is a prevalent issue that frequently leads to youngsters being sent to hospitals. A comprehensive history and physical examination are essential components of a good medical evaluation. Biochemical testing can be helpful in some situations. Understanding the pathophysiology of fluid balance is essential to treating it appropriately. Trials demonstrating the effectiveness of oral glucose-electrolyte solutions in reducing or eliminating the need for intravenous medicine to treat dehydration caused by acute watery diarrhoea (AWD) were conducted mostly on cholera patients were mostly concerned with cholera sufferers. Acute infectious gastroenteritis is the second most common non-traumatic cause of emergency hospitalisation in children aged 1 to 5 years, accounting for approximately 9% of cases (39,410 in 2017), despite the fact that it can frequently be treated as an outpatient procedure (Carsten Posovszky et al., 2020).

The most common path - ogens are viruses (47% rotavirus, 29% norovirus, and 14% adenovirus). **Sylvia Y Ofei, *et al* (2019)** fluid and electrolyte losses from diarrhea and mechanisms of solute cotransport led to development of oral

rehydration solution (ORS), representing a watershed in efforts to reduce diarrheal disease morbidity and mortality. This report reviews the scientific rationale and modifications of ORS and barriers to universal application. **Gabriela G Mosegui, *et al* (2019)** diarrhea causes, annually, approximately 1.7 billion cases and 760,000 deaths worldwide among children under 5 years of age, although these are preventable and treatable. This study aims to assess the cost-effectiveness for the treatment of diarrhea in emergency services in the management of children of acute gastroenteritis with non-severe dehydration. **Genevieve Santillanes, *et al* (2018)** evaluation of dehydration in children and reviews the literature on physical findings of dehydration. Pediatric dehydration is a common problem in emergency departments and wide practice variation in treatment exists. Dehydration can be treated with oral, nasogastric, subcutaneous, or intravenous fluids. According to Germana V. Gregorio et al. (2016), in low-income nations, acute diarrhoea is a major cause of illness and death among children. When someone has acute diarrhoea, glucose-based oral rehydration solution (ORS) helps replenish fluids and stop further dehydration. According to Wendy Barr et al. (2014), family doctors frequently deal with individuals who have severe diarrhoea. Viral gastroenteritis, a self-limited illness, is the most frequent cause. Acute diarrhoea caused by bacteria is more common when there is an increase in travel, comorbidities, and foodborne sickness. About 40 years ago, oral rehydration solution (ORS) was developed as the mainstay of treatment for dehydration brought on by acute infectious diarrhoea (Henry J. Binder et al., 2014).

The basis for ORS's effectiveness is glucose's capacity to promote fluid and sodium absorption in the small intestine through a mechanism that is independent of cyclic AMP. The effects of super disintegrants in Cefixime 50 mg oral disintegrating tablets were developed, evaluated, and compared by KS Remya et al. (2010). For this investigation, sodium starch glycolate and croscarmellose sodium were employed as superdisintegrants. Diggins KC, et al (2008) evaluate current data on the effectiveness of oral rehydration therapy (ORT) in the treatment of mild to moderate dehydration in children. In 1996, Sachdev HP et al. The most significant medical development of this century is oral rehydration solution (ORS), which is the most effective therapy for dehydration brought on by severe diarrhoea and is essential to lowering baby and child.

One of the biggest medical breakthroughs of the century has been thought to be oral rehydration treatment (ORT) using glucose-electrolyte solutions. When it comes to acute diarrheal illnesses of various causes, ORT works well. The World Health Organization's recommended oral rehydration solution (ORS) (Na 90, K 20, glucose 111, and citrate 10 mmol/L) is the most often used ORS globally. Bhan, Mohan, and others (1994) All of the published clinical trials of oral rehydration salts (ORS) based on glycine, L-alanine, L-glutamine, maltodextrin, and rice are reviewed, along with the findings of a number of recently finished but unpublished studies of these formulations that were funded by the WHO. Goepp, J. G. et al. (1993). One of the main reasons youngsters in the US see doctors is acute gastroenteritis. Millions of youngsters in impoverished nations have had their dehydration avoided or reversed by oral rehydration treatment. Diarrhoea is a leading cause of death and illness for babies and children worldwide, according to H B Casteel et al. (1990). Oral electrolyte solutions to treat dehydration were developed as a result of research and understanding of normal and abnormal gastrointestinal physiology. Humans have frequently replaced perceived water losses with oral fluids, either naturally or with a medicinal focus in the form of folk medicines (R M da Cunha Ferreira et al., 1990). Intravenous (IV) fluid replacement therapy was originally launched in the previous century to address. Replacement therapy with intravenous (IV) fluids was formally introduced in the last century for the treatment of patients with cholera. The modern implementation of oral replacement therapy was begun by pediatricians in the 1940s who used electrolyte solutions as maintenance therapy in mildly purging children with diarrhea.

MATERIALS AND METHOD

PREFORMULATION STUDIES

Preformulation is the study of a pharmaceutical substance's physical and chemical characteristics, both by itself and in combination with excipients. The primary objective of preformulation testing is to generate information that will assist formulators in developing stable, bioavailable dosage forms.

IDENTIFICATION OF DRUG

Identification of zinc sulphate was carried out two method Indian Pharmacopoeia and United States Pharmacopoeia.

Test 1: - Test for zinc (limit test)

After dissolving a certain quantity of zinc sulphate in water, a few drops of the sodium sulphide solution of the reagent were added. After a while, a white precipitate of zinc sulphide appeared.

Test 2: - Test for sulfate

Dissolved the sample in water, add the dilute hydrochloride acid and add barium chloride solution in the sample after some time form white crystals barium sulfate. The identity of the drug Zinc Sulphate was confirmed through limit tests for zinc and sulfate ions and optionally through IR Spectroscopy. The drug met the standard specifications as per IP/USP and was found appropriate for further formulation development.

Drug identification was done by the FTIR method. FTIR spectroscopy is a technique used to identify the functional groups present in a molecule by analyzing its infrared absorption spectrum. In the case of zinc sulfate, FTIR can be used to confirm the presence of sulfate (SO_4) and water of crystallization.

SOLUBILITY

Solubility was estimated by keeping the amount of drug constant (1gm) and gradually increasing the amount of solvent (ml) (IP2018). The solubility of drug was determined in various solvent like Water, Ethanol, Methanol, and Methylene di chloride.

DRUG-EXCIPIENTS INTERACTION STUDIES USING FTIR

FTIR is an important modern analytical method for determining the structural features of a molecule as well as identifying the possible interactions between a drug and excipients. Interaction, complexation, or incompatibility may be signaled by indication of changes or loss of characteristic peaks.

PREPARATION OF CALIBRATION CURVE OF ZINC SULPHATE

PREPRATION OF 0.1 N HCL BUFFER

Both water and acidic solutions readily dissolve zinc sulphate. The use of 0.1 N HCl as a gastric mimic (pH-1.2) is commonplace in pharmaceutical practice for the dissolution of water soluble salts like Zinc Sulphate. Use a clean 1000 ml volumetric flask and take carefully 8.5 ml of concentrated hydrochloride acid, transfer the slowly in volumetric flask and add containing 500 ml distilled water well mix. Make up the volume 1000 ml of distilled water and store air tight and proper labelling.

PREPRATION OF STOCK SOLUTION

Use the analytical balance take 100 mg of drug sample transfer in the 100 ml volumetric flask then add 75 to 80 ml of 0.1 N HCL for dissolved the sample then make up the volume 100 ml with 0.1N Hcl. Store airtight and proper labelling.

PREPRATION OF CALIBRATION CURVE IN 0.1 N HCL BUFFER

Use the analytical balance take 100 mg of drug sample transfer in the 100 ml volumetric flask dissolved in minimum amount of 0.1N Hcl in 100 ml volumetric flask then make up the volume 100 ml with 0.1N Hcl.

FORMULATION AND PREPRATION OF ZINC SULPHATE MOUTH DISSOLVING TABLETS

DIRECT COMPRESSION METHOD

Direct compression is the most effective method for powders that combine well and don't require further granulation steps. Direct compression is the most straightforward and affordable tabletting technique. It makes use of widely accessible excipients and standard mixing and tabletting equipment. Direct compression mouth dissolving pills are sturdy and manageable in terms of handling and packaging. The active ingredient in the good mouth feel mouth dissolving tablet must undergo a separate flavour-masking procedure by polymer when using the direct compression technique for medications with an unpleasant taste. (M.E. Aulton, 2002).

PROCEDURE

Mouth dissolving tablet of taste masked Zinc sulphate prepared by direct compression method. Firstly, weighing the all required excipient with the active pharmaceutical ingredient carefully. Passed through the all excipient and active pharmaceutical ingredient with the help of sieve. Active pharmaceutical ingredient passed through # 60 sieve. All excipient passed through #40, magnesium stearate and sodium starch gluconate passed through #60 sieve.Then excipient mixture was properly mixed with dried mass of drug resin complex with the help of blender. The powder bland was lubricated with magnesium stearate. The lubricated material compressed on a 35 station rotary compression machine. Each compressed tablet should be weight 135 mg (calculated amount).

PRE COMPRESSION EVOLUTION OF GRANULES

The dried granules of formulation blends were evolution for micrometrics properties like Bulk density, Tapped density, Angle of repose, and carr's index (% compressibility index).

ANGLE OF REPOSE

Using the funnel method, the granules' angle of repose was ascertained. A certain set of weighted grains was placed in a funnel. A height adjustment was made to the funnel so that its tip barely touches the top of the granule pile. The granules were permitted to freely flow to the surface through the funnel. The following formula was used to calculate the powder cone's angle of repose and estimate its diameter.

$\tan \theta = h/r$

Hence, $\theta = \tan^{-1} h/r$

Where, θ = angle of repose

h = height of the cone

r = radius of the cone base

The flow is deemed good if the angle of repose is less than 20 degrees. The flow is good if the angle of repose is between 20 and 30 degrees. The flow is acceptable if the angle of repose is between 30 and 35 degrees. The flow is quite poor if the angle of repose exceeds 40 degrees.

BULK DENSITY AND TAPPED DENSITY

The density of a powder in its natural condition, including the air spaces between particles, is defined by its bulk density, which is also known as its tapped density. Conversely, taped density is the density that results from mechanically compacting the powder, which closes the air holes and raises the density.

Bulk density (BD) = Weight of the powder / bulk volume of the powder

Tapped density (TD) = weight of the powder / tapped volume

PRESENT COMPRESSIBILITY (CARR'S INDEX)

It can be measure of the potential strength of powder to check the flow property of powder in the hopper. A simple test has been developed flow ability of powder by compare the bulk density and tapped density of granules. It was calculated by using formula.

Carr's index (%) = Pt-Pb/PtX100

Pt = Tapped density

Pb = Bulk density

POST COMPRESSION EVALUATION OF COMPRESSED ZINC SULPHATE DISINTIGRATING TABLET

DESCRIPTION

Verified the 10 tablets in Petri dish and white paper and indusually check the colour and shape of the tablets.

THICKNESS

10 tablets were collect randomly then check the thickness of tablets and check the diameter was measure with the help of digital Vernier calliper.

AVERAGE WEIGHT

Take 20 tablets randomly from composite sample and weighed accurately electronic weighing balance. By using the provided formula, they determine the average weight of the tablets.

Avenge weight = weight of 20 tablets / 20

UNIFORMITY OF WEIGHT

Check the weight of 20 tablets indusually on electronic balance, average weight test, select minimum weight of tablet and maximum weight of tablets and calculate variation of tablets by formula.

(-) variation = minimum weight-average weight / average weight x 100

(+) variation = maximum weight-average weight / average weight x 100

HARDNESS

A calibrated digital hardness tester was used to measure the hardness of six tablets for each formulation. Firstly, press the ON button and then set the unit (kg, neaten) and press the zero button. Between the tester's two jaws, the tablet was supported along its oblong axis.

Round the roller in the present of hardness tester. Generally, a minimum of 4 Kg/cm^2 hardness is considered acceptable for uncoated tablets.

FRIABILITY

For each formulation, to check the friability of 6.50 gm and according to average weight of tablets was determine using the Roche friabillator. Weighing of tablets transfer to friability tester apparatus which revolve at a speed of 25 RPM, dropping the tablets to a distance of 6 inches in each revolution. A sample of pre weighed total tablets was places in Roche friabillator, which was then operated for 100 rounds for 4 minutes. After four minutes, the tablets were cleaned and weighed again. A loss of less than 1% weight is generally considered acceptable. Percent friability (%) was calculated as bellow.

$$\textbf{Friability F (\%)} = (W_0 - W / W_0) \times 100$$

Where,

W0 = Initial weight of tablets

W = Final weight of tablets (after 100 round)

IN-VITRO DRUG RELEASE STUDIES USING THE UV METHOD- DISSOLUTION CONDITIONS

The Zinc Sulphate MDT formulations' eligibility for oral rehydration therapy was confirmed by the in-vitro drug release experiments, which showed that a sizable amount of medicine was released during the first 10 to 15 minutes. The medication was released from the optimized formulation quickly and completely, which is consistent with effective dissolution and disintegration behavior.

DETERMINATION OF UNIFORMITY OF DRUG CONTENT

Choose ten tablets at random from each batch of formulations Crush each pill into a fine powder on its own. Weigh out enough zinc Sulphate monohydrate (20 mg) from each tablet. Dissolve in around 70 mL of 0.1 N HCl after transferring to a 100 mL volumetric flask. Shake or sonicate to guarantee total dissolution. Use 0.1 N HCl to bring the volume up to 100 ml. Use a 0.45 µm membrane filter or Whatman filter paper to filter the mixture on and analyse. Pipette 5 mL of the aforementioned solution into a 50 mL volumetric flask, then dilute with 0.1 N HCl to volume. A UV spectrophotometer can be used to measure the absorbance at 215 nm. Utilizing the zinc Sulphate calibration curve, ascertain the drug content. Every evaluated formulation of zinc Sulphate MDTs complied with pharmacopoeial restrictions, according to the content uniformity test. According to FTIR compatibility results, the medication was found to be evenly distributed throughout the tablets, confirming no drug segregation or incompatibility during manufacturing and bolstering the validity of the formulation method.

IN-VITRO DISINTEGRATION STUDY

Fast-dissolving tablets dissolve when saliva is present in the mouth, but there is a limit to salivary flow, and neither USP nor IP found a disintegration test that could reproduce in vivo conditions. Water was so used. Check the disintegration apparatus proper clean and clear to previous product. Load the 1 tablet in each of the six cylindrical tubes of the basket, using distilled water-maintained 37+-2 ^0C as the immersion fluid and operated apparatus. Wait and check and note the time which all tablets disintegrated completely and recorded the time.

IN-VITRO DRUG RELEASE/ DISSOLUTION STUDY

The capacity of mouth disintegrating tablets (MDTs) to release the medication quickly when they come into touch with saliva or stomach contents determines how effective they are. Since zinc Sulphate dissolves in water, it should ideally exhibit a quick and full release. This investigation also tracks the dissolution performance after formulation, which indirectly supports drug-excipient compatibility.

IN-VIVO TASTE EVALUATION

The taste of tablet was checked by panel method. The study protocol was explained to volunteers and written consent was obtained from them. For this purpose, 10 human volunteers and tablet randomly selected from each batch for the study. Mouth should be properly washed with purified water before tablet was placed on tongue. Observation from volunteers were record for all formulation after placing 15 seconds of the tablet on tongue**. (Suthar A.M et al., 2011).**

STABILITY STUDIES

The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with the time under the influence of a variety of environmental elements, including temperature, light, and humidity, as well as to establish a self-life for the medicinal product or a retest period for the drug substance and suggested storage conditions. In general, a drug product should be evaluated under storage condition that tests its thermal stability and its sensitivity to moisture.

Three types of storage condition are used i.e Tables 6 and 7 display long term, intermediate, and accelerated data. **(ICH Q1A, R2, 2003; Asian Guideline, 2003).**

Table 5: Sample storage condition.

Study	Storage condition	Minimum time period covered by data at submission
Long term	25±2°C/60±5%RH or 30±2°C/75±5%RH	12 month
Intermediate	30±2°C/65±5%RH	6 month
Accelerated	40±2°C/75±5%RH	6 month

Table 6: Sampling intervals.

Storage condition	Sampling intervels
Real time storage	0, 3, 6, 12, 18, 24 month
Accelerated	0, 3, 6 month

ACCELERATED TESTING

The studies designed to increase the rate of chemical degradation or physical change of a drug or drug product by using exaggerated storage condition as part of the formal stability studies.

The optimized formulation (TRA 5) was taken and accelerated stability study was performed by taking suitable quantities of tablets. The tablets were placed in air tight container at 40±2°C/75±5% RH. At suitable sampling interval the samples were withdrawn and evaluated for various parameter.

1. RESULTS AND DISCUSSION

Preformulation studies

Identification of drug

The identity and purity of the drug material are confirmed by the FTIR spectrum of the zinc Sulphate drug sample, which displays all distinctive peaks that closely match the theoretical and IP 2018 reference values.

Table 7: Characteristic Peak with their functional Group.

Peak	Theoretical Value (cm^{-1})	Reference IP 2018(cm^{-1})	Drug Sample (cm^{-1})
O–H Stretching (hydrated water)	3400–3550	3445	3440.95
S=O Symmetric Stretch	1110–1130	1125	1119.52
S=O Asymmetric Stretch	1230–1260	1240	1236.28
Zn–O Bond	450–550	510	507.35
O–H Bending (water of hydration)	1600–1650	1620	1617.68

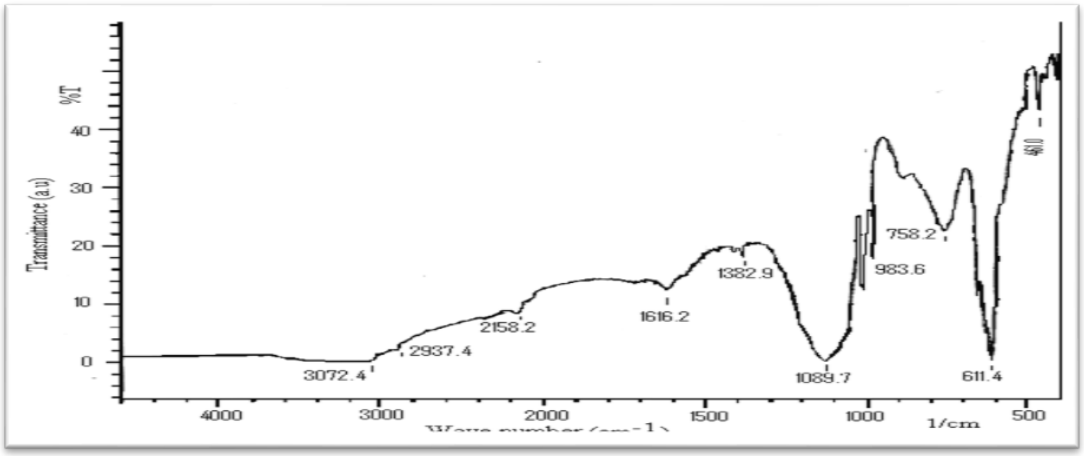

Fig. 3: FTIR Spectra of Zinc Sulphate monohydrate (IP, volume 2, 2018).

SOLUBILITY OF DRUG

Solubility of Zinc Sulphate monohydrate was estimated in different solvents which were describe as follow in table.

Table 8: Results of solubility of drug in different solvents.

Sr. No.	Solvent	Quantity of solvent (ml) used to solubilize 1 gm drug	Solubility Parameter
1.	Water	1.0 ml	Very soluble
2.	Ethanol	1000 ml	Practically insoluble
3.	Methanol	1000 ml	Practically insoluble
4.	Glycerine	100 ml	Slightly soluble
5.	0.1N Hcl	1.0 ml	Freely soluble
6.	Phosphate buffer (pH 6.8)	2.0 ml	Freely soluble

DRUG-EXCIPIENTS INTERACTION STUDIES USING FTIR

FTIR spectra of zinc sulphate monohydrate and its mixture with Cross Povidone Xl-10, Croscarmellose sodium and all excipients used in the formulation are show in figure.

PREPARATION OF CALIBRATION CURVE OF ZINC SULPHATE

Table 9: Calibration curve of zinc sulphate monohydrate in 0.1N HCl.

Sr. No.	Concentration (µg/ml)	Absorbance
1.	2	0.120
2.	4	0.236
3.	6	0.362
4.	8	0.478
5.	10	0.603
6.	12	0.724
7.	14	0.840

EVOLUTION OF MOUTH DISSOLVING TABLET

PRE COMPRESSION EVOLUTION OF GRANULES

The dried granules of different formulation were subjected for evaluation for micrometric properties like angle of repose, bulk density, tapped density, and compressibility index. The results are as shown in table.

Table 10: Results of Pre-Compression Evaluation of Powder Blend.

Formulation	Angle of Repose (θ)	Bulk density (gm/ml)	Tapped density (gm/ml)	Compressibility Index (%)
TRA 1	24.83±0.60	0.93±0.06	1.04±0.04	15.66±020
TRA 2	24.05±0.36	1.07±0.44	1.11±0.05	15.23±0.61
TRA 3	26.40±0.35	1.12±0.20	1.19±0.01	17.00±0.25
TRA 4	21.36±0.43	0.82±005	0.96±0.004	11.90±0.35
TRA 5	21.60±67	0.77±0.45	0.94±0.02	12.06±0.20

The results of evaluation of pre-compression parameters showed (Table 11) that angle of repose varies from 21.60 and Carr's index varies from 12.06. It is category of good flow property. So we can say that all formulation (granules) have the good compressibility which is the basic requirement for the direct compression.

POST COMPRESSION EVALUATION OF COMPRESSED ZINC SULPHATE

Disintigrating tablet

Description

White coloured, uncoated, scored, both sides plain. The prepared tablets of all 5 formulations were subjected to post-compression parameter i.e. thickness, diameter, average weight, uniformity of weight, drug content. All the post-compression parameter of all formulation complies the I.P, 2018 specification of mouth dissolving tablet. The results are shown in table 11.

Table 11: Results of Post-Compression Evaluation of all formulation.

Formulation	Thick-ness (mm)	Dia-meter (mm)	Avg. weight (mg)	Uni-formity Weight (%)	Hard-ness (kg/cm^2)	Fria-bility (%)	Drug Content (%)	DT (sec)
TRA 1	2.3±0.04	7.14±0.014	135.40	-2.2 to +2.6	3.33±0.25	0.19	98.10 to 100.5	190±2.5
TRA 2	2.29±0.08	7.14±0.02	135.10	-2.5 to +3.2	3.1±0.40	0.22	98.50 to 101.5	185±3.0
TRA 3	2.34±0.01	7.13±0.01	135.80	-2.4 to +2.8	2.6±0.25	0.40	99.20 to 101.40	114±5.0
TRA 4	2.6±0.14	7.14±019	135.20	-2.1 to +2.5	2.8±044	0.35	99.00 to 102.0	61±2.6
TRA 5	2.36±0.2	7.12±0.015	135.12	-2.5 to +2.9	3.0±0.32	0.25	99.10 to 101.60	24±2.5

The results of post-compression evaluation of tablet showed that thickness 2.36±0.2 mm and diameter 7.12±0.015mm and hardness 3.0±0.32 kg/cm^2 and DT 24±2.5 sec. so there was no significant change in all these parameters which clearly indicates that blending was uniform. The disintegration time was improved with increase in concentration in Crospovidone XL-10 a super disintegrants, which ultimately affect the dissolution of drug. Formulation TRA 5 showed the best disintegration time in all formulation.

Table 12: Results of In-vitro Drug release study of cumulative percentage drug release of MDT.

Time (min)	CUMULATIVE % DRUG RELEASE				
	TRA 1	TRA 2	TRA 3	TRA 4	TRA 5
2	25.25	28.32	29.87	28.36	31.25
5	66.75	68.45	71.25	68.52	73.52
10	86.25	92.65	92.32	89.65	94.35
15	92.85	98.14	98.10	97.25	98.25

The percent zinc sulphate monohydrate released from mouth dissolving tablet in formulation TRA 1 was found to be 92.85% (minimal) and TRA 5 was found to be 98.25%(maximum) after 15 minutes. So it was concluded that TRA 5 was the optimized formulation contain Crospovidone XL-10 and Croscarmellose sodium with all other excipients which are common for all formulation.

STABILITY STUDIES FOR OPTIMIZED FORMULATION

In view of the utility of TRA 5, formulation tablet of the zinc sulphate monohydrate mouth dissolving dosage form, accelerated stability studies were carried out at 40±2^{o}C/75±5% RH. The protocol of the stability study was in confirmation with the recommendation in ICH documents for the stability testing of the product intend for the global market. After storage formulation (tablets) was subjected for the evaluation of physical parameter like description, thickness, diameter, average weight, weight uniformity, hardness, friability, taste, drug content, disintegration time and in vitro release.

Table 13: Accelerated stability testing results of optimized formulation TRA 5 at the storage condition i.e. 40±2^{o}C/75±5% RH.

Time (Month)	Thick-ness (mm)	Diameter (mm)	Avg. Weight (mg)	Uniformity Of weight (%)	Hardness (kg/cm)	Friability (%)	Drug Content (%)	DT (sec)
0	2.35±0.20	7.11±0.015	135.35	-3.5 to +4.0	3.0±030	0.30	99.05 to 102.2	24
3	2.30±0.008	7.13±0.05	135.30	-2.7 to +3.1	3.2±0.40	0.35	98.6 to 101.60	25
6	2.32±0.01	7.12±0.03	135.15	-3.4 to +2.8	3.2±0.42	0.38	99.15 to 101.35	26

Table 14: stability testing results of in-vitro drug release study of cumulative percentage drug release of MDT.

Time (min)	CUMULATIVE % DRUG RELEASE		
	0 Month	3 Month	6 Month
2	31.25	28.26	22.78
5	73.52	68.32	63.62
10	94.35	89.45	86.22
15	98.25	97.35	95.25

The results of accelerated stability studies showed that there is no significant change in the physical parameter like description, thickness, diameter, average weight, weight uniformity, hardness, friability, taste, drug content, disintegration time and in vitro release. The disintegration time and cumulative percent drug release slightly change but not significant after the six months of the storage condition 40±2^{o}C/75±5% RH. So we can say the optimized formulation (TRA 5) was the stable formulation.

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