CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187

https://zenodo.org/uploads/10077267

https://www.iajps.com/volumes/volume10-october-2023/39-issue-10-october-23/

Available online at: http://www.iajps.com *Research Article*

FORMULATION STUDIES OF TABLETS OBTAINED FROM SOLID DISPERSION AND SOLVENT EVAPORATION OF METRONIDAZOLE POWDER

Ordu John I[1] * Onyinyechi N[2] and Okafo Sinoduko E**
Department of Pharmaceutics and Pharmaceutical Technology,
Faculty of Pharmaceutical Sciences, University of Port Harcourt, Nigeria.
** Department of Pharmaceutics and Industrial Pharmacy,
Faculty of Pharmacy, Delta State University, Abraka
Email address: okafose@delsu.com

Abstract:
Metronidazole (MTZ) is an anti- microbial/ anti-protozoal drug poorly soluble in aqueous medium. The solubility was enhanced by dispersion in poly ethylene glycol at a controlled temperature and recrystallized with n-hexane then resultant powder washed severally with distilled water to obtained a clear slightly colloidal/ nano sized powder. The recrystallized powder was analyzed for purity using the thermo-gravimetric method and possible structural loss and interaction applying the FTIR, particle size analysis using scanning electron microscopy(SEM) then compared for powder flow and compressibility index with untreated metronidazole powder. The crystallized and non-crystallized mtz powders were formulated into granules and tagged batch A and B respectively with same concentrations of excipients then eventually compressed into tablets. Various physico-technical properties of the granules were analyzed for both batches and there after compressed to tablets. The resulting tablets were determined for hardness, friability, dissolution and content of active ingredient while the flow rate of granules from the batches were 4.59±0.05959 and 3.24±0.0082, angle of repose (θ) at 32.9±0.3399 and 35.1±0.2625, Hausner's ratio 1.20±0.024 and 1.17±0.033, friability at 0.05 and 0.38, compressibility index 0.16±0.012 and 0.15±0.024, % drug release within 60 minutes at 110.75±12.510 and 127.5±20.241 while percentage(%) drug content was 80.2 and 105 respectively for the batches A and B.

***Key words**: metronidazole powder, tablets, solid dispersions, solvent evaporation, formulation studies*

Corresponding author:
Ordu John I,
Department of Pharmaceutics and Pharmaceutical Technology,
Faculty of Pharmaceutical Sciences, University of Port Harcourt, Nigeria.
** Email address: john.ordu@uniport.edu.ng*
Phone No: 234±8037211706

QR code

Please cite this article in press Ordu John I et al, ***Formulation Studies Of Tablets Obtained From Solid Dispersion And Solvent Evaporation Of Metronidazole Powder,*** *Indo Am. J. P. Sci, 2023; 10 (10).*

INTRODUCTION:

Oral administration of drugs is the most desired route for many pharmaceutical products due to its significant advantages over other formulations. It is the most commonly used route due to its greater stability, ease of administration, high patient compliance, accuracy of doses, cost-effectiveness and flexibility of dosage form design [1].

The bioavailability and therapeutic effectiveness of a drug administration of oral route depends on several factors which includes aqueous solubility, drug permeability, dissolution rate, systems metabolism and susceptibility to efflux mechanisms. When a drug is administered orally, the drug has to first dissolve in the gastrointestinal fluids before it can be absorbed into the blood stream and circulate to its site of therapeutic action [2].

Solubility is one of the most important parameter to achieve the desired drug concentration in systemic circulation and to attain the required pharmacological response.

The most causes of low oral bioavailability are poor solubility and low permeability. Dissolution is a function of the solution and surface area of a drug and may be the rate determining step for drug absorption, bioavailability and onset of therapeutic activity. Poorly water soluble drugs often require highest doses to reach therapeutic plasma concentrations after oral administration, also they have slow drug absorption that leads to inadequate and variable bioavailability. The improvement of drug solubility thereby its oral bioavailability remains one of the most challenging aspect of the drug development process especially for an oral-drug delivery system. Drug solubility and bioavailability enhancement are the important challenges in the field of formulation of pharmaceuticals [3].

Solubility study: The solubility of a substance fundamentally depends on the solvent used as well as temperature and pressure. The extent of solubility of a substance in a specific solvent is measured as the saturation concentration where adding more solute does not increase its concentration in the solution. Solubility is a major challenge for formulation scientist and for any drug to be absorbed, it must be present in the form of solution at the site of absorption. Various techniques are used for the enhancement of the solubility of poorly soluble drugs [4].

Solid Dispersion Technology: Solid dispersion refers to as a group of solid products consisting of at least two components e.g. hydrophilic matrix and a hydrophobic drug where the drugs had been dispersed molecularly or in the amorphous state. The matrix may either be a crystalline or amorphous form. If solid dispersion product is exposed to an aqueous media, the carrier will dissolve and the drug is being released as fine colloidal particles with an enhanced surface area that produces a higher dissolution rate and also improve bioavailability. The problem of solubility made pharmaceutical industry to search for approaches that will enhance drug solubility using both the chemical, physical and carrier-based techniques (Vasconcelos et al., 2007) [6]. The chemical methods involve, the molecular modification of drug structure which results in the formation of new chemical salts or additive conjugate with varied pharmacokinetic and pharmacodynamics profiles [7], the physical methods work by the principle of decreasing the particle size and increasing the contact surface area which will lead to enhancement of the drug solubility. Another formulation approach that has been used to enhance the solubility are the production of lipid vessicles and/or surfactants based liquid systems; or carrier based solid formulations [8].

The solid dispersions “depict” one of the most interesting approaches as it has presented a reduction in the size of particles, improved wettability, solubility, high porosity and also has enhanced drug stability [9].

The improvement of drugs dissolution from solid dispersions is based mainly on three mechanisms as: particle size reduction, increased surface area and the wettability of the drugs which is improved upon by direct contact with the hydrophilic matrix and also by the conversion of the crystalline state or more soluble amorphous state.

The selection of a carrier influences the dissolution characteristics of the dispersed drug because the dissolution rate is one of the component from which the surface is being affected by the other component in the multiple component mixtures hence various hydrophilic carriers such as polyethylene glycols (PEGs) polyvinyl pyrrollidone (PVP), hydroxypropyl methylcellusose (HPMC) gums, sugar, mannitol and urea have been used for the improvement of dissolution characteristic and bioavailability of poorly soluble drugs [10].

Methods of enhancing availability of poorly water-soluble drugs

Several techniques have been successfully employed to enhance the solubility, dissolution and

bioavailability of poorly water-soluble drugs and they include: particle size reduction, micronization and nanosuspensions [11]

Precipitation technique: In this technique, the drug is being dissolved in a solvent after which it is added to anti-solvent in order to precipitate the crystals. The precipitation techniques are not applicable to drugs which are simultaneously poorly soluble in aqueous and non-aqueous media.

Spray Drying Method: This involves the dissolving of drug and polymer in an organic solvent and then spray drying the solution. The solubility of active pharmaceutical ingredient (API) in solvent, in the spray drying is crucial to ensure a readily scalable and viable process. The spray drying dispersion enhances oral absorption of poorly water soluble drugs by attaining and sustaining a supersaturated concentration of drug in the gastro intestinal fluid.

Hot Melt Extrusion/Fission Method: In this method, the physical mixture of a drug and water soluble carrier are heated directly until the two mixture melts. The melted mixture is cooled, solidified rapidly in an ice bath with rigorous stirring then final solid mass is crushed, pulverized and sieved then compressed into tablet aided by a tableting agents.

Lipid Based Delivery Systems: This method involves the establishment of the solubility range of the drug in various lipid and once this is formed, the dry/lipid mixture can sustain drug concentration in targeted environment. The lipid formulation can be compressed because of the number of additive required to meet performance objective.

Solvent Evaporation Method: In this method, both the drug and the carrier were dissolved in a common solvent and evaporated under vacuum to produce a solid substance [12]

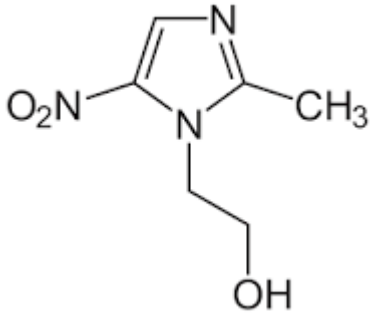
Nano Formulation: Nano formulations of medicinal drugs have attracted the interest of many researchers for drug delivery application. These nano formulations enhances the properties of conventional drugs and are specific to the targeted delivery site. Dendrimers, Polymeric nanoparticles, liposomes, nano-emulsion and micelles are some of the formations that are gaining prominence in pharmaceutical industry for enhanced drug formulation. Wide varieties of synthesis method are available for the preparation of Nano formulation to deliver drugs in biological system. The choice depends on the size, shape and precipitate formulation, biochemical properties of drug and the targeted site. (Jaison Jeevanandam et al) [13].

The development of nano formulation produces the ability to improve drug residence time, increase permeability and bioavailability of the drug, reduce degradation of unstable drug and well tolerated by the patient compared to the conventional drug.
Nano formulation varies in size from 10-100mm and the drug is dissolved, entrapped, encapsulated or attached to the drug carrier**.**

Metronidazole as a Drug
Metronidazole is a nitro-imidazole derivatives, it is an antimicrobial and antiprotozoal drug that has been used as drug of choice in the treatment of extra luminal amoebiasis and also for infectious disease caused by an anaerobic bacteria. It effectively eradicates intestinal and extra intestinal tissue infections. It has both anaerobic, antibacterial and anti-helicobacter activity. Metronidazole is an enzyme inhibitor and it is a typical representative of the imidazole derivatives (1, 3 diazole).

Another area of application of metronidazole is the eradication of helicobacter pylori in the duodenal ulcer and/or stomach ulcer. Metronidazole is used in a triple therapy bismuth based drugs the drug that blocks H_2 receptors and inhibit the proton pump[14].

Description of Metronidazole
The substance of metronidazole is a crystalline powder of light yellow or white in colour, it is slightly soluble in water, acetone and ethanol (1:100) this can limit its use in some cases and cause difficulties technologically in the creation of new drugs and thereby reduction in their bioavailability.
Metronidazole is sparingly soluble in water but it has an oral bioavailability of 93-95% and it is extensively metabolized by the liver.
Chemistry



2- Methyl =-5 metronidazole-1-ethanol
Fig.1: Structure of metronidazole

Mechanism of Action of Metronidazole
Metronidazole acts by disrupting the DNA's helica structure thereby inhibiting the bacterial nucleic acid synthesis and eventually resulting in bacterial cell death [15].

Pharmacokinetics of Metronidazole: It is well absorbed from the intestinal tract, absorption is delayed but not reduced by food. It is well distributed in the body fluids and with a half-life of about 7 hours

Drug Interaction: Metronidazole is a weak inhibitor of alcohol dehydrogenase thus alcohol ingestion should be avoided. Metronidazole interferes with the metabolism of warfarin and may potentiate it's anticoagulant activity while Phenobarbital and corticosteroids lowers metronidazole metabolism. Metronidazole is recommended in pregnancy [16].

Tablet: This also known as pill is defined as the solid unit dosage form or medicament with suitable excipients. It comprises of a mixture of active substances and excipients usually in powder form, pressed or compacted into a solid dose. Tablets are prepared either by molding or by compression of the excipient which may include diluents, binders or granulating agents, glidants (flow aids) and lubricants to ensure effective tableting [17].

Aim of the study
To formulate, study and evaluate the physico chemical properties of tablets resulting from solid dispersion and solvent evaporation of metronidazole powder.

MATERIALS:
Metronidazole powder, propylene glycol, n-hexane, distilled water, Poly vinyl pyrollidone (PVP), gelatin, starch, talc, 0.IM HCl, magnetic stirrer (hotplate), oven, tableting machine (erweka), disintegrating machine, dissolution apparatus, friabilator, weighing balance (electronic weighing balance), sieve of various mesh size.

Methods
A 30g of the pure mtz powder was weighed and transferred into a beaker using analytical weighing balance and dispersed in 100ml of propylene glycol for solubilization after being placed on hot plate and stirred at a temperature of $60^{O}C$ for one hour. The solubilized mixture was removed and allowed to cool then about 50ml of n-hexane was added and reheated for recrystallization of the sample. The recrystallized powder was allowed to cool after being left for 12 hours for proper recovery of the material. The mixture was filtered by passing through a muslin cloth and the recovered powder washed severally with distilled water to remove the debris, odor and presence of organic substance then filtered and dried in an oven at $40^{o}C$. The dried colloidal metronidazole was formulated into tablets (Batch A) and alongside with another batch B of pure untreated powder adopting the wet granulation method.

Formulation of Metronidazole
Metronidazole granules were formed both for the hydrolyzed (batch A) and the non-hydrolyzed (batch B) powders according to the formulae in table 1. The amount of each of the ingredients that was required for formulation of the wet granules was calculated and weighed. Thereafter, some amounts of the exo-excipients including, magnesium stearate, talc, certain percentage content of starch was also calculated and weighed. The granules were formed by a wet granulation technique and the damp mass of mtz and components were passed through a 2 mm sieve and dried for 20 minutes then subsequently passed through a 1mm sieve and after which the exo- excipients were added and mixed.

Table 1: Formulation of Tablet

MATERIALS	BATCH A (% content)	BATCH B (% content)
Metronidazole powder	86.27	86.27
PVP	0.48	0.48
Starch	1.69	1.69
Gelatin	0.24	0.24
Magnesium stearate	0.24	0.24
Starch	0.118	0.118
Talc	0.96	0.96

Flow Properties of Metronidazole Powders

Angle of repose (θ)

The angle of repose was determined using fixed funnel method. Funnel is fitted vertically with height of 2mm above the surface. The opening end of funnel was closed with the thumb while the granule (2.0g) was introduced. The granule was released from the funnel orifice and the height of the powder was noted. The radius of the heap was measured and the angle of repose (θ), calculated using the formula.

Angle of repose, (θ) = h/r ---------- (1)

Carr's Index

This is a test to evaluate the bulk density and tapped density of powder and the rate at which it can flow, pack and have good compression. It is calculated using the formula.

$$\text{Compressibility index} = \frac{\text{Tapped density - bulk density}}{\text{Tapped density}} \text{---} (2)$$

Hausner ratio

Hausner's ratio is an index of ease of powder flow. It is the ratio of true density to bulk density. The lower the value of Hausner's ratio, the better is the flow property.

It is calculated by the following formula

$$\text{Hausner ratio} = \frac{\text{Tapped density}}{\text{Bulk density}} \times 100 \ldots\ldots\ldots (3)$$

Bulk density

A 15g of granules was weighed and transferred into a dry graduated measuring cylinder without the application of stress. The volume occupied was noted for both granules in triplicate and determined as:

$$\text{Bulk density} = \frac{\text{mass}}{\text{bulk volume}} \times 100 \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (4)$$

Taped density

Same measure as in the bulk density determination was weighed and transferred into a dry graduated measuring cylinder. The measuring cylinder was tapped on a padded table surface for up to a certain number of times. The tapping was done until a steady volume was obtained and the number of taps was noted. This was done for both granules in triplicates and tapped density was calculated as:

$$\text{Tapped density} = \frac{\text{mass}}{\text{Tapped volume}} \times 100 \ldots\ldots (5)$$

The flow rate

The flow rate was determined using a modification of the Jones and Pilpel method. Here, 15g of the granules was weighed and poured into a funnel that was clamped at a height of 2cm above a flat surface platform while the orifice of the efflux tube was closed with a metric rule to prevent premature discharge of the granules. On removal of the metric rule, the time it took the granules to completely discharge from the funnel was determined and this was done in triplicate for each of the granules.

$$\text{Flow rate} = \frac{\text{mass of granules}}{\text{time to completely discharge}} \ldots\ldots\ldots (6)$$

FTIR Study

The IR analysis of the sample was carried out for qualitative compound identification and possible compound interaction. Transmittance was measured from wave number 4000 cm-1 to 400cm-1 using Happ-Gensel anodization.

Particle size analysis

Particle size of the crystalized powder was analyzed using the scanning electron microscopy (SEM) and by X-ray diffraction method.

Characterization of Metronidazole Tablets

The metronidazole tablets were characterized 24hrs after being tableted for their physical properties (friability, weight uniformity, hardness and thickness), disintegration, content of active ingredient and percentage drug release.

Physical appearance

The tablets were visually examined to determine their color, shape and possible defects such as chipping or capping.

Uniformity of weight

The metronidazole tablets were checked for variation in tablet weight by randomly selecting and individually weighing 20 tablets from each batch of the formulation and comparing to the mean.

Hardness/crushing test

Through a process of random selection, 10 tablets from each batch of the formulations was collected and a model TBH hardness tester (Erweka, Germany) was used to determine pressure at which each tablet diametrically caps.

Disintegration time

The disintegration time of the metronidazole tablets were determined by randomly selecting six tablets from each batch of the formulation and putting each tablet from a given batch into each of the six cylindrical holes of a model ZT-122 disintegration machine (Erweka, Germany). The disintegration medium was 700 ml of 0.1N HCl held in a 1 L beaker that was immersed in a water bath. The temperature of

both the medium and bath were maintained at 37±0.5ºC. The machine was switched on and disintegration was said to have taken place when the entire tablet has been broken down into small fragments which are not retained on the mesh. If any mass is retained, it must not be a firm or core of the tablet used for the test.

Friability Test

Ten tablets were randomly selected from each batch of the tablet formulations and freed of dust, collectively weighed (W1) and placed into the drum of the friability tester, model TAR 200 (Erweka, German). The machine was operated and the drum caused to rotate at 25 rpm for 4 min. the tablets were collected, de-dusted, reweighed (Wf) and the percentage friability (F) calculated.

$$\text{Friability test} = \text{initial weight} - \frac{\text{final weight(Wf)}}{\text{Initial weight(W1)}} \times 100$$

Thickness Test

Ten tablets were picked at random from each batch of the metronidazole tablets. The thickness and diameter of the tablets were individually determined using a micrometer screw gauge. The mean and standard deviation for each determination was recorded.

Determination of maximum absorption of metronidazole

A 100 mg/ml stock solution of metronidazole was prepared by dissolving 100 mg of the reference mtz powder in sufficient quantity of phosphate buffer (pH 7.2) in a 100 ml volumetric flask, and made up to the 100 ml volume using same solvent. A portion of the prepared solution was scanned in a UV spectrophotometer model 6405 (Jenway, UK) to obtain the maximum wavelength (λmax) of the powder.

Standard calibration (Beer's plot)

Serial dilutions of the stock solution were made to obtain concentrations of 0.02, 0.04, 0.06, 0.08. The absorbance reading of the diluted metronidazole solutions were obtained using the spectrophotometer at λmax of 241nm. A plot of the absorbance readings against the different concentrations was made from which standard calibration curve was determined.

Dissolution of metronidazole

The dissolution of metronidazole and its release profile from the tablets were carried out using a six station dissolution apparatus DT 600 (Erweka, German). A tablet from each batch was individually placed in 900 ml of phosphate buffer (pH 7.2) solution contained in a 1 L flask placed in a water bath at temperature maintained at 37±0.5ºC with a paddle speed set at 10.0 rpm. Five ml samples were withdrawn from the test media at every 10 min and filtered through a filter paper. Five ml of fresh 0.1N of the buffer maintained at the same temperature was used to replace the withdrawn sample after each sampling time. The filtrates were scanned at wavelength of 241nm and the absorbance readings obtained were converted to concentrations using the standard established calibration curve equation.

Assay/content of active ingredient determination

Assay of the metronidazole tablets was done using the British Pharmacopoeia method. Ten tablets each of the metronidazole tablets formulated were randomly selected and weighed collectively to determined their total weight. They were pulverized to very fine powder and the quantity equivalent to the mean weight of one tablet was taken and dispersed in a 0.1N media solution in a 100 ml volumetric flask. The contents were properly shaken; after which they were filtered through a filter paper. A hundred-fold dilution of the filtrate was made and its absorbance determined at a wavelength of 241nm. The absorbance result was then imputed into the established calibration curve equation and the concentration determined.

RESULTS:

Table 2: Results of Physicochemical/Physic technical Properties of Granules and Tablets

	Sample A			Sample B		
	Mean	**Std. deviation**	**CV**	**Mean**	**Std. deviation**	**CV**
Flow rate (g/s)	**4.59**	**0.0579**	**0.0126**	**3.24**	**0.0082**	**0.0025**
Angle of repose (θ)	**32.9**	**0.3399**	**0.0457**	**35.1**	**0.2625**	**0.0348**
Bulk density	**0.42**	**0.0052**	**0.0120**	**0.52**	**0.0066**	**0.0127**
Tapped density	**0.52**	**0.0132**	**0.0256**	**0.62**	**0.0090**	**0.0145**
Hausner's Ratio	**1.20**	**0.024**	**0.020**	**1.17**	**0.033**	**0.028**
Compressibilty Index	**0.16**	**0.012**	**0.075**	**0.15**	**0.024**	**0.161**
Disintegration Time (sec.)	**9.49**	**0.538**	**0.057**	**9.85**	**0.297**	**0.030**
% drug released in 60 minutes	**110.75**	**12.510**	**0.113**	**127.5**	**20.241**	**0.159**
Uniformity of weight (g)	**206.3**	**4.7668**	**0.231**	**206.3**	**7.369**	**0.0357**
Tablet thickness (cm)	**0.034**	**0.0049**	**0.1441**	**0.031**	**0.0020**	**0.0645**
Tablet diameter (cm)	**0.0082**	**0.0023**	**0.0281**	**0.0081**	**0.0020**	**0.0247**
Tablet Hardness	**5.15**	**0.3905**	**0.0758**	**5.17**	**0.4082**	**0.0790**
Friability	**0.05**			**0.38**		
% Active ingredient	**80.2**			**105**		

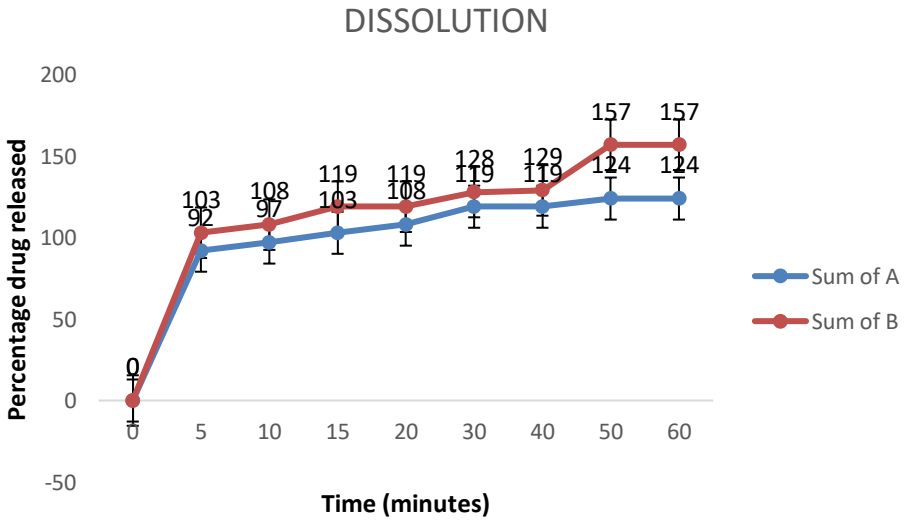


Fig. 2: Percentage drug released gainst Time (minutes)

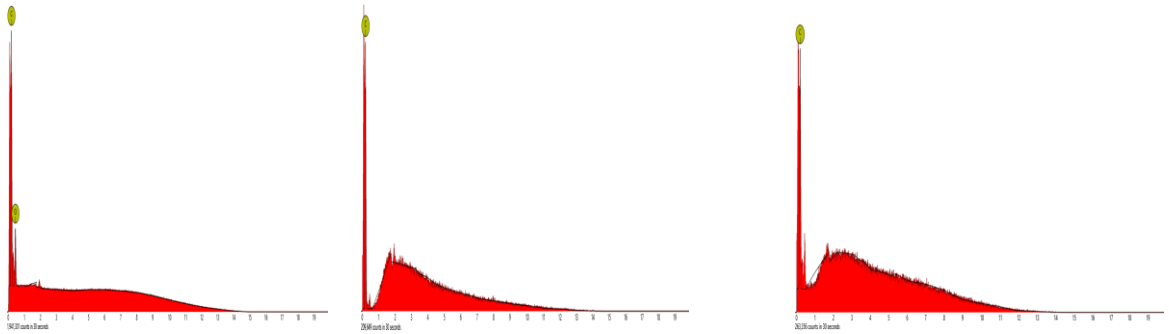


Fig. 3: X-ray analysis of re-crystallized metronidazole

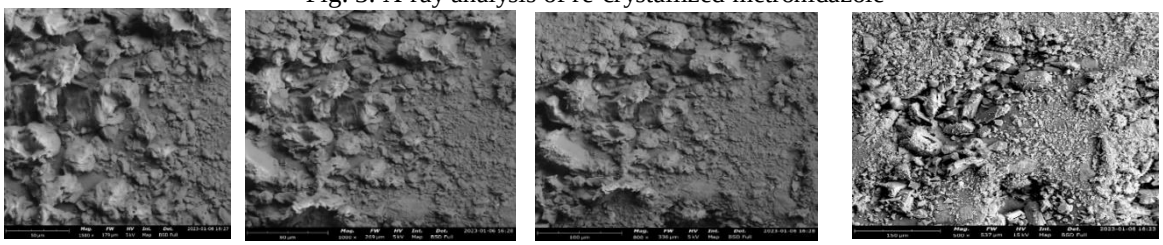


Fig. 4: Particle size analysis of re-crystallized metronidazole powder

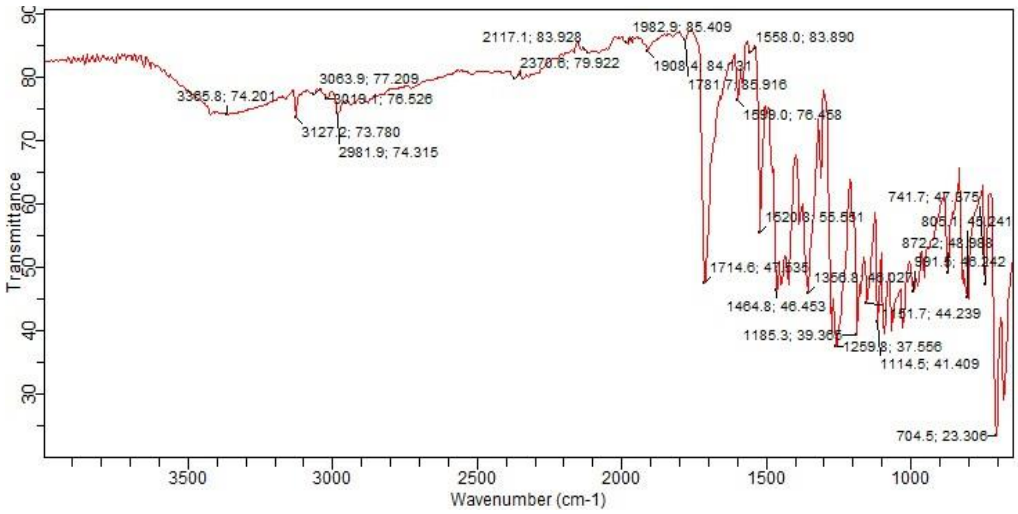


Fig 5: FTIR of re-crystallized Metronidazole powder

DISCUSSION:

The flow properties of any given powders and granules can be evaluated directly through flow rate and the indirectly by method involving angle of repose, Hausner's ratio, compressibility index and porosity. From the results of the study, it could be observed that increase in size of particles relative to the funnel orifice may or may not increase the flow rate. Also the sieve size of 1.0mm aperture showed increase in the flow rate while the powders with larger particles size have greater bulk density as in Batch B and with increased flow rate than that with smaller particle size powder as in batch A.

The greater the crystalline nature of the powder the greater gravitational force required to make it flow and the lesser the force of cohesion which resist the flow of powder particle. The particle size analysis as observed from the result of the scanning electron microscopy (SEM) (fig. 4), showed that the solid dispersion and solvent extraction method adopted for the metronidazole powder, assisted in the particle size reduction though still within the micro meter size range but the particle size of the recrystallized mtz powder was smaller than the untreated powder (batch B).

X-ray diffraction is a powerful nondestructive technique for characterizing crystalline materials. It provides information on structures, phases, preferred crystal orientations (texture), and other structural parameters, as average particle size, crystallinity,

strain, and crystal defects. Analysis of powder by XRD provides important information that is complementary to various microscopic and spectroscopic methods, such as phase identification, sample purity, crystallite size, and, in some cases, morphology. The peak broadening of XRD relates to the widths of the peaks, whereas the relative intensities relate to the height, although XRD patterns for spherical particles of nanoscale dimensions will have the same relative intensities as the bulk material, but the peaks will be broadened [18] but in this study, based on the result as in fig 3., the peaks were not broadened signifying that the particles were not on the nano meter size range. This also buttressed the fact that the broadening in the peaks of the XRD patterns arises due to finite size of the crystals hence if there is presence of infinite size crystals, the peaks in the XRD pattern appears as very sharp but as size get reduces peak broadening increases.

FTIR spectra reveal the composition of solids, liquids, and gases. The most common use is in the identification of unknown materials and confirmation of production materials [19]. The FT-IR spectrum of the treated metronidazole showed the vibrational peaks at 2981, 1558, and 1529 cm-1 that were attributed to C-H stretching, C=C (carbonyl ring) stretching and C=N (imidazole ring) stretching, respectively, comparable to the un-treated powder and signifying absence of extraneous materials with no interaction amongst the formulation materials.

From the physico-chemical characterization results as shown in Table 2, powders from batch A has a lower tapped density (0.516±0.00262g/ml) compared to those in batch B with a tapped density of (0.612±0.0g/ml). The high bulk density as observed in powders of batch B is due to the crystalline nature and presence of void spaces and pores within the particle bed compared to the lower size, less porous and tightly packed powders of batch A [20]. The angle of repose of both batch A and B are 33.97^{O} and 35.1^{o} respectively, hence the powders had good flow properties according to the reference standard.

Relative to the reference standard, compressibility index (CI) of < 10% and Hausner's ratio of 1.00-1.11 is said to have an excellent flow. From the study, the CI obtained was 0.1657±0.012, Hausner's ratio 1.20±0.024 for batch A and that of batch B are CI, 0.15 ±0.024 and Hausner's ratio, 1.17±0.033 respectively, and from this, it means that the powders have good flow properties but fair compressibility characteristic.

The weight uniformity test as performed showed that the samples of the batches obtained complied with the reference standard, as weight uniformity is a function of granules quality, flow and machine performance.

A relationship exists between the tablet compression and tablet thickness. Tablet thickness is determined by the diameter of the die, the amount of the fill permitted to enter the die leading to the compaction characteristics of the fill material and the pressure applied during compression to manufacture tablets of uniform thickness during the drug formulation [21]. Tablet thickness is important for tablet packaging as very thick tablets could result after packaging either in blisters or plastic containers more so as tablet thickness is determined by the diameter. From the study, the thickness of the tablet range between 0.30mm and 0.40mm for batch A and 0.30 and 0.35mm for batch B which shows that there was no much variation in the thickness of the tablets resulting from both batches.

Generally, tablets should be sufficiently hard to resist breaking during normal handling, packaging and shipping and yet soft enough to disintegrate properly after swallowing. Hardness of the tablet is controlled by the degree of the pressure applied during the compression stage.

Tablet hardness was measured using Mosanto hardness tester and the tablets were generally placed between two planes, one of which moves to apply sufficient force to cause fracture especially on conventional round tablet. Tablet hardness ranges between 5 to 10kg/cm^2, limit ± 5% and from the results obtained, the tablets hardness met the optimum specification suitable for official use.

Friability test mimics the force of cohesion or sliding effect of tablet against each other during the packaging, shipping and handling process, and according to the official book (USP) the percentage permissive loss is ≤1%. From the study, the tablets upon subjection to friability test had a loss of 0.05 and 0.33% for batch A and B respectively and this indicates that the tablet passed the test and hence assumed to be capable of withstanding possible stress and could remain stable over a long period of time upon storage under recommended condition. Also the different values of the friability of the two batches clarifies the packing nature of the powders in each batch where it was assumed that powders in batch A, are more tightly packed than that for batch B.

The official book (USP) specified that the disintegration time for coated tablet should not be

greater than 30 minutes for six tablets while the (British Pharmacopoia) specified that the disintegration time for uncoated tablet should not exceed 15 minutes for six tablets. From result obtained, the mean disintegration time for six tablets for batch A was 9.85±**0.538** while that of batch B was 9.65±0.297 minutes and this shows that the formed tablet disintegrated within acceptable range and therefore good for ingestion since disintegration is the first physical change observed for a drug when it enters into the body.

The drug release curve as in fig. 2 shows that sample A had faster drug release rate than sample B. This could be attributed to the decrease particle size of the API as a result of the solvent dispersion and evaporation technique adopted. Considering the percentage of active content, batch A, had lower value than that obtained in batch B. This could be as a result of the effect and impact of the formulation process where powders in batch A was subjected to solid dispersion and solvent evaporation while that of batch B did not pass through any process rather only the pure drug sample was used for the formulation.

CONCLUSION:

Poor solubility and low permeability of drugs results in their low bioavailability in the systemic circulation thereby reducing their pharmacological response or action. It is therefore imperative for the use of carriers or adoption of recrystallization and solid dispersion technique as applied with the n-hexane recovery of poly ethylene glycol dispersed metronidazole powder to enhance particle size reduction, permeability and drug bioavailability. This technique has helped to improve or enhance the dissolution characteristic of poorly aqueous dispersible drugs like metronidazole and hence improve the bioavailability and therapeutic efficacy of such class of molecular entities.

REFERENCES:

1. Bahman Homayun, Xueting Lin, and Hyo-Jick Choi . (2019): Challenges and Recent Progress in Oral Drug Delivery Systems for Biopharmaceuticals. *Pharmaceutics*;11(3):129. doi: 10.3390/pharmaceutic s11030129.

2. Rong Lu , Yun Zhou , Jinqian Ma , Yuchen Wang , Xiaoqing Miao (2022): Strategies and Mechanism in Reversing Intestinal Drug Efflux in Oral Drug Delivery. *Pharmaceutics.* 14(6):1131. DOI: 10.3390/pharmaceutics14061131

3. Anagha Bhakay , Mahbubur Rahman , Rajesh N Dave , Ecevit Bilgili (2018): Bioavailability Enhancement of Poorly Water-Soluble Drugs via Nanocomposites: Formulation–Processing Aspects and Challenges. Pharmaceutics. 10(3):86. doi: 10.3390/pharmaceutics10030086.

4. Amol S. Deshmukh1*, Kundan J. Tiwari and Vijay R. Mahajan1(2023): Solubility Enhancement Techniques for Poorly Water-SolubleDrugs. Review Article *(9):* Pg 3701-3706

5. Anjana MN, Joseph J and Nair SC (2023). Solubility Enhancement Methods- A Promising Technology for Poorly Water Soluble Drugs. *International Journal of Pharmaceutical Sciences Review and Research* 20(2): 127-134

6. Teófilo Vasconcelos , Bruno Sarmento , Paulo Costa Drug (2007): Review: Solid dispersions as strategy to improve oral bioavailability of poor water soluble drugs. Discovery Today; Volume 12, Issues 23–24, , Pages 1068-1075.

7. Faten Farouk, Rehab Shamma (2019): Chemical structure modifications and nano-technology applications for improving ADME-Tox properties, a review. *Arch Pharm. Chemistry in Life sciences*. Volume 352, Issue2. https://doi.org/10.1002/ardp.201800213

8. Indhu A. Chacko, Vivek M. Ghate, Leonna Dsouza, Shaila A. Lewis (2020): Lipid vesicles: A versatile drug delivery platform for dermal and transdermal applications. *Colloids and Surfaces Biointerfaces*; Volume195. https://doi.org/10.1016/j.colsurfb.2020.1 11262

9. Aftab Modi1 and Pralhad Tayade2 (2006): Enhancement of Dissolution Profile by Solid Dispersion (Kneading) Technique. *AAPS PharmSciTech)*; 7 (3): Pg1-6

10. Xingwang Zhang, Huijie Xing, Yue Zhao, and Zhiguo Ma (2018): Pharmaceutical Dispersion Techniques for Dissolution and Bioavailability Enhancement of Poorly Water-Soluble Drugs. *Pharmaceutics.* 10(3): 74. doi: 10.3390/pharmaceutics10030074

11. Swati Sareen, George Mathew, and Lincy Joseph (2012): Improvement in solubility of poor water-soluble drugs by solid dispersion. *Int J Pharm Investig.* 2(1): 12–17. doi: 10.4103/2230-973X.96921.

12. Tomasz Urbaniak and Witold Musiał (2019):. Influence of Solvent Evaporation Technique Parameters on Diameter of Submicron Lamivudine-Poly-ε-Caprolactone Conjugate Particles. Nanomaterials (Basel); 9(9): 1240. doi: 10.3390/nano9091240

13. Jaison Jeevanandam , Yen San Chan , Michael K Danquah . (2016): Nano-formulations of drugs: Recent developments, impact and challenges.

Biochimie 128-129:99-112. doi: 10.1016/j.biochi.2016.07.008.
14. Kazunari Murakami , Tadayoshi Okimoto, Masaaki Kodama, Ryugo Sato, Koichiro Watanabe, Toshio Fujioka (2008): Evaluation of three different proton pump inhibitors with amoxicillin and metronidazole in retreatment for Helicobacter pylori infection. *J Clin Gastroenterol.* 42(2):139-42. doi: 10.1097/MCG.0b013e31802cbc1a.
15. Simon A Dingsdag, Neil Hunter (2018): Metronidazole: an update on metabolism, structure–cytotoxicity and resistance mechanisms. . *Journal of Antimicrobial Chemotherapy*, Volume 73, Issue 2: Pages 265–279, https://doi.org/10.1093/jac/dkx351
16. Ibrahim Dighriri , Ahmed Mobarki , Naif Althomali , Khalid Alqurashi , Othman Daghriri , Bashaer Bin Howimel , Izdihar Alahmad , Rawan Alsaadi , Manar Alsufyani , Manar Balobade , Reem Altemani , Bayader Alatawi , Wejdan Sharoufna , Taif Almuntashiri , Sultan Almushawwah (2021): Detect Drug Interactions with Metronidazole. *Journal of Pharmaceutical Research International*, Volume 33, Issue 47A, Page 597-604. DOI: 10.9734/jpri/2021/v33i47A33049
17. Sachin S. Gaikwad & Sanjay J. Kshirsagar (2020): Review on Tablet in Tablet techniques.. *Beni-Suef University Journal of Basic and Applied Sciences* volume 9, Article number: 1 (2020)
18. J. Madhavi (2019): Comparison of average crystallite size by X-ray peak broadening and Williamson–Hall and size–strain plots for VO^{2+} doped ZnS/CdS composite nano powder. Review Paper. *SN Applied Sciences*; volume 1, Article number: 1509.
19. S. Ramukutty, E. Ramachandran (2012): Crystal growth by solvent evaporation and characterization of metronidazole. Journal of Crystal Growth; Volume 351, Issue 1, Pages 47-50. https://doi.org/10.1016/j.jcrysgro.2012.04.017
20. Eman Hussain Elmubarak, Zuheir Abdelrahman Osman Mohammed Abdelrahman (2021): Formulation and evaluation of solid dispersion tablets of furosemide using polyvinylpyrrolidone k-30. International journal of Current Pharmaceutical research; vol 13, issue 2 doi: https://doi.org/10.22159/ijcpr.2021v13i2.41554
21. Odeku OA, Awe OO, Popoola B, Odeniyi MA, Itiola OA. Compression & mechanical properties of tablet formulations containing corn, sweet potato and cocoyam starches as binders, Pharm. Technol., 2005; 29(4): 82-90.

Note* The [DATA TYPE] data used to support the findings of this study are included within the article.
Any further enquiry, the email address (john.ordu@uniport.edu.ng) could be contacted