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Original Research Article

Formulation of sustained release matrix tablets of metronidazole using sintering technique

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Abstract

Purpose: The study was conducted to formulate and evaluate controlled release metronidazole matrix tablets by thermal sintering using *Irvingia gabonesis* (IG) gum as binder.
Methods: Metronidazole granules were prepared by wet granulation technique using 10 %w/w each of the extracted IG and tragacanth gums and the prepared granules were evaluated for micromeritic properties. The granules were compressed into tablets and some of the prepared tablets were subjected to thermal sintering at 50 and 60 ºC for 1, 3 and 5 h. Both the sintered and unsintered tablets were evaluated for physicotechnical properties.
Results: The results revealed that the prepared metronidazole granules were free flowing with angles of repose of ≤ 28º and Carr's indices ≤ 15 %. An increase in tablet hardness occurred with increase in sintering temperature and time while the percentage friability decreased. The in-vitro dissolution profile of the prepared controlled release matrix tablet of metronidazole showed that the optimum drug retardation occurred in tablets sintered at 60 ºC for 5 h.
Conclusion: The study has revealed that IG gum at a concentration of 10%w/w possesses good binding properties and can be utilized in the formulation of controlled release matrix tablets of metronidazole by thermal sintering.

Keywords: Thermal sintering, *Irvingia gabonesis*, matrix tablets, metronidazole

Indexing: Index Copernicus, African Index Medicus

Introduction

Recently, design of extended release dosage forms have gained significant attention over the conventional dosage forms due to its numerous benefits such as patient convenience and adherence to therapy, maintenance of a steady level of drug over a long time interval, reduction of the dosing frequency of the drug etc [1].

Sintering can be defined as the bonding of adjacent particle surfaces in a mass of powder or in a compact, by the application of heat [2]. Conventional sintering involves the heating of solid material in a controlled environment at a temperature below its melting point under atmospheric pressure [3]. Heating in the presence of transient or stable liquid phases and under pressure (hot-pressing), high frequency induction heat sintering, spark plasma sintering and microwave sintering are variations of the convectional sintering and are recent advances in sintering technologies [4]. Sintering affects the physicotechnical properties of granules, tablets dissolution rate as well as the release kinetics. A study conducted by Uhumwangho and Murthy on the effects of sintering on the physicotechnical parameters of unsintered and sintered matrix granules of diltiazem hydrochloride revealed that the sintered matrix granules had significant higher Hardness-Friability Index (HFI) value [5]. More so, there was an increase in HFI values with increase in temperature and duration of sintering. In another study, it was showed that sintering strengthens a compact by increasing the points of contact and

solid-bond formation between particles within the compact and this result in increased tensile strength of the compacts formulated after sintering for 24 h at four different temperatures [6]. Kondaiah and Prakash, investigating the effect of sintering on the hardness of polymeric matrix tablet of theophylline, reported an increase in tablet hardness with increase in sintering temperature and time [7]. Similar results have also been reported by Rao *et al* [8].

Sintering also affects the disintegration time of a tablet which is dependent on the relative magnitude of the forces exerted by the disintegrant and the binding forces within the tablet. For a tablet to disintegrate in water, the forces exerted by the disintegrant must overcome the binding forces within the tablet.

Pilpel and Esezobo studied the effect of sintering on the disintegration time of acetaminophen and oxytetracycline tablets and reported that a higher tensile strength and longer disintegration time was exhibited by tablets sintered at a higher temperature [9] and was this confirmed by Ando *et al* [10]. When they observed an increase in disintegration time for ethyl amino benzoate tablets after sintering and attributed this increase to the enhanced tensile strength of the tablet after sintering.

Metronidazole belongs to the class of drugs referred to as nitro imidazole antiprotozoal drug. It has a molecular formula of $C_6H_9N_3O_3$ and a molecular weight of 171.15 g/mol. Metronidazole is a pale yellow odourless crystalline powder with melting point of 159 - 163 ºC. It is slightly soluble in water (10 mg/ml at 20 ºC). It is the drug of choice in the treatment of mild to moderate *Clostridium difficile* associated diarrhoea [11,12]. It is an antimicrobial agent that has potent antibacterial activity against anaerobes, including *Bacteriodes* and *Clostridium* species [13]. It is well absorbed after oral administration and peak plasma concentration is reached in 1 - 3 h. It has a low protein binding of 10 - 20 % with half-life of 7.5 h (unchanged drug). It can also be administered topically, rectally and intravenously. Metronidazole is metabolized in the liver and excreted mainly through the urine.

IGgum is a natural polymer gotten from Irvingia seeds (*Irvingia gabonesis*) and it is soluble in hot water but insoluble in ethanol, acetone and cold water. Irvingia gum has been reported to be used as a matrix former in the formulation of floating drug delivery system, binders in tablet formulations, and even as a suspending agent [15]. The aim of this study was to formulate sustained release of matrix tablets of metformin using sintering technique.

Methods

Extraction of Irvingia gabonesis (IG) gum

IG gum was extracted by the method described previously by Momoh *et al* [14].

Preparation of metronidazole granules

The formulae used in the preparation of the metronidazole granules by wet granulation technique is shown in Table 1. Two batches were prepared using IG and tragacanth gums at concentration of 10 %w/w each. The metronidazole powder was wet massed with appropriate amount of binder solution and triturated thoroughly in a mortar. The damp mass was screened through a laboratory sieve of aperture size 850 µm and dried at 60 ºC for 30 min in a hot air oven (Kottermann, Germany). The dried granules were passed through another laboratory sieve of aperture size 710 µm. Magnesium stearate and talc were added extra-granularly.

Table 1: Formula for the preparation of metronidazole matrix tablet

Ingredients	Quantities/tablet
Metronidazole	400 mg
Irvingia or tragacanth gum	10 %w/w
Talc	1.0 %

Evaluation of the prepared granules

The prepared granules were evaluated for pre-compression parameters like bulk and tapped densities, Carr's index, Hausner's ratio and angle of repose.

Bulk density

A sample of granules (10 g) was weighed into a clean, dry 50 ml measuring cylinder, and the volume occupied by the granules was recorded as bulk volume. The bulk density was determined using equation 1.

$$Bulk\,density = \frac{Weight\,of\,granules}{Volume\,of\,granules} \quad \ldots. \quad (1)$$

Tapped density

Granules (10 g) were weighed into a clean, dry 50 ml measuring cylinder. The cylinder was then tapped 100 times from a constant height and the tapped volume was read. The tapped density was determined using equation 2.

$$Tapped\,density = \frac{Weight\,of\,granules}{Tapped\,volume\,of\,granules} \ldots. \quad (2)$$

Carr's index and Hausner's ratio

The Carr's index was determined as described by Carr, 1965. It was calculated by dividing the difference between the values of tapped and bulk densities by the value of tapped density. The result was expressed as percentage using equation 3.

$$Carr's\,index = \frac{Tapped\,density - Bulk\,density}{Tapped\,density} \times 100 \ldots \quad (3)$$

Hausner's ratio was determined by calculating the ratio of tapped density to bulk density using equation 4.

$$Hausner's\,ratio = \frac{Tapped\,density}{Bulk\,density} \quad \ldots. \quad (4)$$

Angle of repose

The flow properties of the granules were evaluated using the fixed funnel method to determine the static angle of repose. A funnel was fixed with its tip at a given height, above a flat horizontal surface on which a paper was placed. 10.0 g of granules was carefully poured through a funnel with the tip of the funnel blocked with the index finger. The finger was removed and the granules were allowed to fall freely on the paper under the influence of gravity to form a heap. The circumference of the base of the heap of the granule was drawn and the radius (r) was measured in centimetre (cm). The angle of repose of the granule was calculated by using equation 5. Angle of repose is expressed mathematically as;

$$\theta = \tan^{-1} h/r \quad \ldots. \quad (5)$$

Where; θ = Angle of repose, h = Height of the heap (cm), r = Radius of the base of the heap in (cm)

Compression of granules into matrix tablets of metronidazole.

Controlled release matrix granules equivalent to 400 mg of metronidazole were compressed into tablets using a lubricated single punch tableting machine (Type F3 Manesty machine, UK) fitted with a concave punch and die set at a compression pressure of 30 arbitrary unit on the load scale. A constant pressure was maintained for all the batches of metronidazole produced. Tablets containing 400 mg metronidazole were produced and collected, dusted and stored in an air tight jar containing activated silica gel as a desiccant.

Sintering of the prepared tablets

The prepared metronidazole matrix tablets formulated with irvingia and tragacanth gums were divided into 7 subgroups, each comprising of 20 tablets. For the irvingia gum batch, tablets from three subgroups (IG1, IG2 and IG3) were subjected to thermal sintering at 50 ºC in a hot air oven for 1, 3 and 5 h, respectively. Tablets from another three subgroups (IG4, IG5 and IG6) were also sintered at 60 ºC for 1, 3 and 5 h, respectively. The last subgroup tablets (IG) were retained as unsintered tablets. Same procedure was repeated for tablets prepared using tragacanth gum and designated as TG, TG1, TG2, TG3, TG4, TG5 and TG6.

Evaluation of tablets

The controlled release matrix tablets of metronidazole were evaluated for the following;

Hardness test

Five (5) tablets were selected at random from each subgroups and the hardness of the tablets was determined using the Monsanto hardness tester. The lower plunger was placed in contact with the tablet and the pointer was adjusted to the zero mark. The plunger was then forced against a spring by tuning a threaded bolt until the tablet fractured diametrically. As the spring was compressed a pointer rides along a gauge in the barrel to indicate the force which was expressed in KPa.

Friability test

The friability of five (5) tablets from each subgroup was determined using a Roche friabilator (Erweka Germany). Ten tablets were initially weighed and placed in the drum of the friabilator, revolving at 25 rpm. After 4 min, the tablets were taken out and reweighed after removal of fines by dusting the tablets. The percentage weight loss of the tablets was calculated using equation 6.

$$Friability = \frac{Initial\ weight - Final weight}{Initial\ weight} \times 100 \ldots. \quad (6)$$

Dissolution study

The release rate of metronidazole from tablets was determined using an Erweka Dissolution Apparatus (Type DT6, Erweka GmbH, Heusenstamm, Germany). The dissolution test was performed using 900 ml of 0.1 N HCl, at 37 ± 0.5 °C as the dissolution medium and a paddle speed of 100 rpm. A sample of the solution (5 ml) was withdrawn from the dissolution apparatus at various time intervals up to 10 h and replaced with fresh dissolution medium at 37 ± 0.5 °C. Samples were filtered and diluted to a suitable concentration with 0.1 N HCl solution. Absorbances of these solutions were measured at a wavelength of 276 nm, using a 1cm cell and 0.1 N HCl as blank solution. The determination was carried out in triplicate and the mean results recorded. The corresponding amount of metronidazole released at any time t, was then computed from the standard calibration curve.

In-vitro drug release kinetics

The pattern of release of metronidazole matrix tablets was determined by subjecting data obtained from their dissolution profile to different models of drug release kinetics. The models used are, zero order (cumulative amount of drug released vs. time), first order (log % drug unreleased vs. time), Higuchi model (% drug released vs. square root of time) and Korsmeyer and Peppas (log % drug released vs. log time) which are the most frequently reported drug release kinetics from solid dosage forms [16-19]. The equations for the release kinetic models are;

Zero order: $m = k_o t$ …. (7)
First order: $\log m_1 = \log m_o - 0.43\, k_1 t$ …. (8)
Higuchi model: $m = k_H t^{1/2}$ …. (9)
Korsmeyer & Peppas: $\log\%m = \log k_2 + n \log t$ … (10)

Where; m = % drug released in time t
m_1 = *Residual % of drug in time t*
m_o = *initial amount of drug (100 %) at the beginning of the first order release*
k_o, k_1, k_H *and* k_2 *are release rate constants for zero order, first order, Higuchi model and Korsmeyer and Peppas release models respectively.*
n = diffusional release exponent.
The correlation coefficient (r^2) of each release model was calculated and the dissolution profile was considered to have followed a particular release order if the correlation coefficient value was ≥ 0.95 [20].

Statistical analysis

Results obtained were reported as mean ± standard deviation (SD). Comparison of all the results obtained was done using student t-test and p values < 0.05 were considered to be statistically significant.

Results

Micromeritic properties of the formulated metronidazole granules

The micromeritic properties of matrix granules of metronidazole prepared using IG and tragacanth gums are presented in Table 2. The Carr's indices of the metronidazole matrix granules prepared using IG and tragacanth gums were 14.70 ± 1.0 % and 13.89 ± 1.1 % respectively thus indicating that the granules possessed good compressibility characteristics. The granules of metronidazole prepared with IG and tragacanth gums had Hausner ratio ≤ 1.17 ± 0.01 and this indicates that all the granules exhibited good flow properties. Metronidazole granules prepared with IG and tragacanth gums had angle of repose of ≤ 28 ± 1.1° which indicates that the granules exhibited excellent flow.

Tablet hardness

The result of sintering temperature and time on the physical properties of the tablets formulated with IG and tragacanth gums are presented in Table 3. The hardness of the metronidazole matrix tablets formulated with tragacanth gum was significantly higher than tablets formulated with IG gum. For instance, the hardness of unsintered metronidazole matrix tablet formulated with IG gum was 2.82 ± 0.36 KPa while the hardness of unsintered metronidazole matrix tablet formulated with tragacanth gum

Table 2: Micromeritic properties of metronidazole matrix granules prepared with *Irvingia gabonesis* and tragacanth gums

Parameters	Formulations	
	***Irvingia gabonesis* gum (IGG)**	**Tragacanth gum (TG)**
Bulk density (g/cm^3)	0.5882 ± 0.02	0.5556 ± 0.01
Tap density (g/cm^3)	0.6896 ± 0.02	0.6452 ± 0.03
Carr's index (%)	14.70 ± 1.0	13.89 ± 1.0
Hausner's ratio	1.17 ± 0.01	1.16 ± 0.02
Angle of repose (°)	27.90 ± 1.1	27.80 ± 1.0

was 4.03 ± 0.31 KPa, thus indicating a statistically significant difference in their hardness values (P > 0.05).

Tablet friability

The percentage friability of metronidazole matrix tablets produced using IG gum was observed to be significantly higher than the tablets produced using tragacanth gum. For instance, the percentage friability of unsintered metronidazole matrix tablet formulated with IG gum was 2.44 ± 0.03 % while the hardness of unsintered metronidazole matrix tablet formulated with tragacanth was 1.91 ± 0.04 %.

Table 3: Physicotechnical properties of metronidazole tablets prepared with *Irvingia gabonesis* and tragacanth gums sintered at different temperatures and times

Formulations	Parameters		
	Hardness (H) (Kg/cm^2)	**Friability (F) (%)**	**H-F ratio**
IG	2.82 ± 0.36	2.44±0.03	1.16
IG1	3.21 ± 0.35	2.26±0.03	1.42
IG2	3.52 ± 0.35	1.91±0.03	1.84
IG3	4.02 ± 0.39	1.36±0.02	2.96
IG4	3.60 ± 0.39	1.62±0.03	2.22
IG5	3.81 ± 0.26	1.40±0.02	2.72
IG6	4.08 ± 0.30	0.94±0.01	4.34
TG	4.03 ± 0.31	1.91±0.04	2.11
TG1	4.36 ± 0.30	1.49±0.02	2.93
TG2	4.68 ± 0.21	0.95±0.02	4.93
TG3	5.10 ± 0.29	0.67±0.02	7.61
TG4	4.92 ± 0.38	0.92±0.04	5.35
TG5	5.48 ± 0.23	0.52±0.01	10.54
TG6	6.82 ± 0.31	0.47±0.01	14.51

Note; IG = Unsintered tablets, IG 1, IG2 and IG3 = tablets sintered at 50ºC for 1, 3 and 5 h respectively. IG4, IG5 and IG6 = tablets sintered at 60 ºC for I, 3 and 5 h respectively.
TG = Unsintered tablets, TG1, TG2 and TG3 = tablets sintered at 50 ºC for 1, 3 and 5 h respectively. TG4, TG5 and TG6 = tablets sintered at 60 ºC for I, 3 and 5 h respectively.

In-vitro dissolution profile of prepared tablets

The results of the dissolution profile of unsintered and sintered tablets of metronidazole prepared with IG and tragacanth gums are shown in Table 4. It was observed that the unsintered tablets formulated with IG and tragacanth gums were able to retard the release of the drug for 6 and 8 h respectively while the sintered tablets were able to retard the drug release for 10 h. This indicates that the drug release pattern varies as the sintering temperature and duration increases. For instance, the maximum amount of drug released (M_∞) for tablets formulated with IGgum sintered at 50ºC and 60ºC for 3 h were 97.09 % and 93.0 1% respectively. While the maximum amount of drug released (M_∞) for tablets formulated with tragacanth gum sintered at 50 ºC and 60 ºC for 3 h were 95.08 %, and 90.03 % respectively with maximum time of drug release (T_∞) being 10 h for each tablet.

Release kinetics of the metronidazole matrix tablets

Data from dissolution profile of the prepared matrix tablet were subjected to Zero order, First order, Higuchi, and Korsmeyer and Peppas models in order to determine the kinetics of drug release. The results of the various release kinetics for matrix tablets prepared with IG and tragacanth gums are shown in Table 5.

Discussion

The hardness of the tablets was found to increase with increase in sintering temperature and duration and this can be as a result of increase in solid bond formation between the particles within the tablets. For instance, the hardness of metronidazole tablet formulated with IG gum sintered for 1 and 3 h at a temperature of 50 ºC were 3.21 ± 0.35 KPa and 3.52 ± 0.35 KPa respectively while metronidazole tablets prepared using tragacanth gum sintered for 1 and 3 h at a temperature of 50 ºC were 4.36 ± 0.30 KPa and 4.68 ± 0.21 KPa. There was a

significant difference in their hardness value ($P > 0.05$).

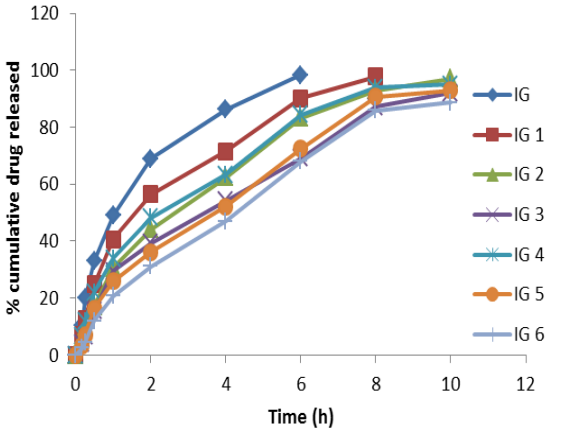

Figure 1: *In-vitro* dissolution profile of metronidazole tablets prepared with 10% *Irvingia gabonesis* (IG) gum

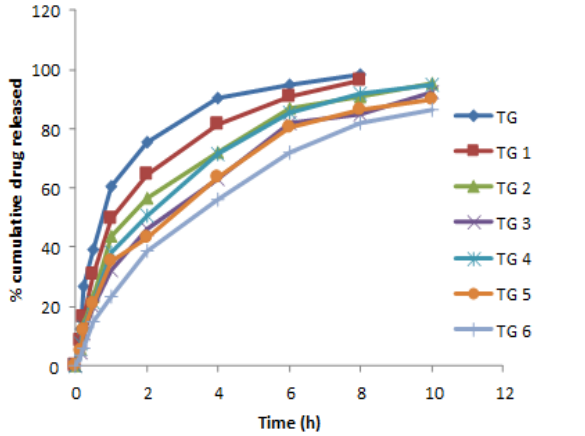

Figure 2: *In-vitro* dissolution profile of metronidazole tablets prepared with 10% tragacanth gum (TG)

Table 4: Dissolution parameters of metronidazole matrix tablets formulated with *Irvingia gabonesis* and tragacanth gums

Formulations	M_∞ (%)	t_∞ (h)	M_∞/t_∞(%hr^{-1})
IG	98.43	6	16.41
IG1	97.78	8	12.22
IG2	97.09	10	9.71
IG3	92.05	10	9.21
IG4	95.10	10	9.51
IG5	93.01	10	9.30
IG6	88.71	10	8.87
TG	98.08	8	12.26
TG1	96.13	8	12.02
TG2	95.08	10	9.51
TG3	92.43	10	9.24
TG4	94.78	10	9.48
TG5	90.03	10	9.00
TG6	86.32	10	8.63

Note: M_∞ (%) = maximum amount released, t_∞ (h) = maximum time of release, M_∞/t_∞ (%hr^{-1}) = ratio of maximum amount released to maximum time of release.

IG = Unsintered tablets. IG1, IG2 and IG3 = tablets sintered at 50 ºC for 1, 3 and 5 h respectively. IG4, IG5 and IG6 = tablets sintered at 60 ºC for 1, 3 and 5 h respectively.

TG = Unsintered tablets. TG1, TG2 and TG3 = tablets sintered at 50 ºC for 1, 3 and 5 h respectively. TG4, TG5 and TG6 = tablets sintered at 60 ºC for 1, 3 and 5 h respectively.

Table 5: Correlation coefficient and release kinetics of metronidazole matrix tablets from formulations with *Irvingia gabonesis* and tragacanth gums

Formulations	Models							
	Zero order		First order		Higuchi		Peppas	
	R^2	K_o	R^2	K_1	R^2	K_H	R^2	n
IG	0.6720	19.98	0.9669	-0.28	0.9769	42.54	0.6720	0.47
IG1	0.7763	14.66	0.9364	-0.21	0.9855	36.04	0.7320	0.57
IG2	0.8567	11.72	0.8374	-0.20	0.9879	32.02	0.8235	0.49
IG3	0.8903	10.70	0.9382	-0.15	0.9758	30.09	0.8639	0.51
IG4	0.7967	11.78	0.9334	-0.20	0.9900	32.84	0.7843	0.64
IG5	0.9152	10.88	0.8909	-0.16	0.9724	29.59	0.8763	0.72
IG6	0.9437	10.21	0.9005	-0.13	0.9519	27.81	0.8936	0.62
TG	0.7368	10.94	0.8852	-0.24	0.9569	41.24	0.6541	0.52
TG1	0.8196	11.37	0.9679	-0.23	0.9542	37.93	0.6947	0.58
TG2	0.8408	9.24	0.9790	-0.18	0.9632	33.33	0.7465	0.61
TG3	0.8986	9.17	0.9605	-0.16	0.9840	30.64	0.8467	0.76
TG4	0.8743	9.39	0.9737	-0.18	0.9797	32.76	0.8115	0.69
TG5	0.8945	8.96	0.9828	-0.14	0.9839	30.46	0.7832	0.73
TG6	0.9313	8.90	0.9555	-0.12	0.9801	27.76	0.9128	0.83

Also, the hardness values of unsintered and sintered (5 h at 60 ºC) metronidazole tablets formulated with IG gum were 2.82 ± 0.36 KPa and 4.08 ± 0.30 KPa respectively, while the hardness values of unsintered and sintered (5 h at 60ºC) metronidazole tablets formulated with tragacanth gum were 4.03 ± 0.31 KPa and 6.82 ± 0.31 KPa respectively ($P > 0.05$). This is an indication that the hardness of tablet formulation is affected by increase in sintering temperature and duration. Generally, the hardness of tablet formulations increase with increase in sintering time and temperature in accordance with some previous studies [7,8].

The percentage friability of tablets were observed to be affected by sintering temperature and time as percentage friability of the formulated tablets decreased with increase in sintering temperature and time. For instance, the percentage friability of unsintered metronidazole matrix tablets formulated with IG gum and those sintered at 60 ºC for 5 h was 2.44 ± 0.03 % and 0.94 ± 0.01 % respectively while the percentage friability of unsintered metronidazole matrix tablets formulated with tragacanth gum and those also sintered at 60 ºC for 5 h was 1.91 ± 0.04 % and 0.47 ± 0.01 % respectively. At particular sintering temperature for different durations, the percentage friability was also observed to decrease.

It was also observed that the maximum amount of drug released (M_∞) reduced with an increase in duration of sintering. For instance, the maximum amount of drug released for tablets formulated with IG gum sintered at 60 ºC for 3 and 5 h were 93.01 % and 88.71 % respectively while the maximum amount of drug released for tablets formulated with tragacanth gum sintered at 60 ºC for 3 and 5 h were 90.03 and 86.32 % respectively which is in accordance with previous studies carried out by Rao and Murthy [21] showing that an inverse relationship exist between rate of release of drug from tablet formulation and sintering time, that is, release rate decreases as sintering time increases. The decrease in release rate of drug on sintering can be attributed to the increase in tablet hardness which led to increase in points of contact and solid-bond formation between particles within the compact thus resulting in decreased penetration of the compact by the dissolution medium. The decrease in release rate of drug on sintering can also be attributed to the movement of polymer chain as well as the redistribution of the polymer throughout the tablet matrix structure resulting from melting and re-solidification of the polymer as the sintering time and temperature increases [22].

Figures 1 and 2 shows that the matrix tablets prepared with IG and tragacanth gums did not follow a zero order release pattern which is the desired model for controlled release drug delivery system. The plot of zero order showed poor linearity with regression values ranging from 0.67 – 0.94 for matrix tablets prepared with IG gum and 0.74 – 0.93 for tablets prepared with tragacanth gum thus indicating that the amount of drug release is not constant throughout the time of release and also depends on the amount of drug left in the system. It was also observed that the r^2 value for zero order release kinetics increased with increase in sintering temperature and duration.

A fair linearity was observed when the data obtained from dissolution profile of the prepared matrix tablets were subjected to first order release model with regression values between 0.84 - 0.97 for tablets prepared with IG gum and 0.89 - 0.98 for tablets prepared with tragacanth gum. Thus, implying that the amount of drug remaining in the system determines the amount of drug that is released. Diffusion mechanism is generally the mechanism of drug release from matrix tablets prepared with hydrophobic polymer [23]. Diffusion of drugs depends on the concentration of the drug as it relates to the transportation of the drug from the dosage matrix into the *in-vitro* dissolution medium.

The release kinetics of the prepared matrix tablets tends towards Higuchi release model as the plot of data obtained from *in-vitro* release profile of the tablets showed a high linearity with regression coefficient (r^2) values between 0.952 - 0.990 for tablets prepared with IG gum and 0.954 - 0.984 for tablets prepared with tragacanth gum. When compared with the other release models analyzed, the release kinetics showed more consistency with the Higuchi model which gave higher regression values. Therefore, the release of drug from matrix tablets is most likely controlled by the Higuchi model which states that the amount of drug release is dependent on the square root of time.

Data from the *in-vitro* release profile of the prepared matrix tablets of metronidazole were also fitted into Korsmeyer-Peppas kinetic

equation to obtain the diffusional release exponent 'n' which gives an indication of the mechanism of drug release. The values of the diffusional release exponent 'n' confirmed that the mechanism of drug release from the prepared matrix is most likely diffusion controlled due to the consistency of r^2 values obtained from the Higuchi release model. The diffusional release exponent of the tablets prepared with IG gum was between 0.47 - 0.72 and 0.52 - 0.83 for tablets prepared with tragacanth gum. This indicates that the dominant mechanism of drug release from the prepared matrix tablets is diffusion and this is in accordance with previous studies on matrix tablets prepared with different polymers carried out by Sarfraz *et al* [24] and Uhumwangho and Okor [25]. The diffusional release exponent (n) of all the prepared matrix tablets were > 0.45 thus indicating that their release mechanism was by non-Fickian diffusion.

Conclusion

Controlled release matrix tablets of metronidazole were successfully formulated in this study by thermal sintering using IG gum as polymer. Based on the results of the study it can be concluded that IG gum at a concentration of 10 %w/w can be utilized in the formulation of controlled release metronidazole tablets by thermal sintering technique and the rate of drug release is a function of the sintering temperature and time. Finally, a controlled release matrix tablet of metronidazole that can retard drug release for up to 10 h has been formulated by thermal sintering technique using IG gum as matrix former.

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Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them. UMU conceived and designed the study, supervised the laboratory works, and also reviewed the manuscript, ACO co-supervised the laboratory works, analysed the data and prepared the manuscript and OEG carried out the laboratory work.

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