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Citrus Sinensis Peel Pectin: A Novel Binder in Erythromycin Tablet Formulation

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Abstract
The aim of this study was to do comparative evaluation of citrus sinensis peel pectin as a pharmaceutical excipients (binder) in erythromycin tablet formulation. The orange peel pectin was extracted from the peel of citrus sinesis, dried, milled and the phytochemicals determined. The granules formulated were evaluated for micromeritic properties. The granules were compressed to tablets at the compression pressure of 30N/m^2 and later evaluated for hardness, friability, disintegration time, dissolution studies and release kinetics.
The extracted orange peel pectin was found to contain flavonoids, carbohydrates and reducing sugar. However, alkaloid, anthraquinone, saponin, cardiac glycoside, terpenoid and tannin were found to be absent. The different batches of formulated erythromycin granules were free flowing with angle of repose between 20.07 ± 3.74 to 20. 82 ± 1.51., bulk density (0.43 ± 0.03 to 0.53 ± 0.02); tapped density (0.51 ± 0.05 to 0.61 ± 0.03); compressibility index (8.12 ± 3.57 to 13.93 ± 6.20); Hausner's ratio (1.14 ± 0.07 to 1.25 ± 0.19) and flow rate (0.55 ± 0.11 to 0.94 ± 0.13). All formulated erythromycin tablets were uniform in weight. Their hardness were satisfactory (4.5 ± 0.02 to 6.7 ± 0.05 kg/cm^2); friability (0.40 ± 0.12 to 0.91 ± 0.10%). Most of the tablets disintegrated within 15 minutes, except those formulated with 10% of the binders with Acacia 10% $\frac{w}{v}$ (20.1 ± .02 minutes), corn starch mucilage (CSM) 10%$\frac{w}{v}$ (21.4 ± 0.03) and orange peel pection (OPP) 10%$\frac{w}{v}$ (25.4 ± 0.05 minutes) respectively. Increase in the binder concentration resulted in a corresponding increase in hardness and disintegration time, but decrease in percentage friability. The dissolution of all batches of erythromycin tablets fitted into the Higuchi model release kinetics. Orange peel pectin exhibited good binding property comparable to those of the standard Acacia and Corn starch mucilage.

Key Words: *Orange, Pectin, Erythromycin Tablets, Acacia, Higuchi.*

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I. Introduction

Plant derived polymers have evoked increased interest due to their diverse applications as pharmaceutical excipients and also in cosmetics, textiles, paints and paper-making (Tushar S,t al., 2018). These natural polymers are relatively preferred over the synthetic ones because they are biocompatible, cheap, and easily available with low or no toxicity (Kulkarni *et al*., 2005; Femi-Oyewo *et al*., 2004). They are used as binding, thickening, emulsifying agents, and as matrices for sustained release of drugs in pharmaceutical industries (M Ravindrakullal Reddy, Kopparam Manjunath, 2013). Pectin is a naturally occurring biopolymer that is finding increasing applications in the pharmaceutical and biotechnology industry (Aina *et al*., 2012; Tiwari, 2017; Shekhar and Makode, 2012). The choice of a suitable binder for a tablet formulation require extensive knowledge of the relative importance of binder properties for enhancing the strength of the tablet and also of the interactions between the various materials constituting a tablet. The orange is the fruit of various citrus species in the family Rufaceae. The orange originated in a region comprising Southern China, Northeast India, and Myanmar (Morton, 1987); the earliest mention of the sweet orange was in Chinese literature in 314 BC (Xu, Q *et al*., 2013). In 2017, about 73 tonnes of oranges were grown worldwide with Brazil producing 24% of the world total, followed by China and India (FAO Statistics, 2018 – Food and Agriculture Organization of the United Nations). The orange tree is an evergreen, flowering tree, with an average height of 9 to 10 m. Its ova leaves, alternately arranged are 4 to 10 cm long and have crenulate margins. It is a multifunctional constituent contained in the cell wall of terrestrial plants. Plant and their products have always been a source of various

drugs and excipients used in pharmaceutical formulations. The benefits of pectin, a naturally occurring polysaccharide are increasingly appreciated by scientists and consumers due to its biodegradability (Tobias *et al*., 2017).

Erythromycin is an antibiotic used for the treatment of a number of bacterial infections such as respiratory tract infection, skin infections, chlamydia infections, pelvic inflammatory disease, and syphilis (The American Society of Health- System Pharmacists, 2015).

The aim of this study therefore was to extract pectin from dried orange fruit peels and to evaluate its binding properties in the formulation of erythromycin tablet relative to other standard binding agents such as acacia gum and corn starch mucilage respectively.

II. Materials And Methods

Materials:

Erythromycin stearate BP powder, Acacia gum BP, Lactose BP and Talc BP powders were sourced through Sonitex (Nig) Ltd, Benin City, Edo State, Nigeria. Orange fruits (citrus sinensis) were purchased from a local market at Okada, Edo State.

Method:

The sweet orange fruits (Figure 1) were sorted, washed and peeled. The peels (Figure 2) were sun-dried for 4 days and milled into a coarse powder using an automatic grinding machine (GX-390, 13HP, Nigeria) and sieved into fine powder using a 25 BSS mesh-sieve and stored in a clean labeled air-tight container for further analysis (Figure 3).

Extraction of Orange Peel Pectin:

Orange peel powder (250 gm) was weighed and carefully poured into a 2 liter round bottom flask. Acidified water (2 liters of 0.5 N HCl) adjusted to a pH of 2.3 was measured and added to the orange peel powder in the flask, and placed on a reflux condenser set to a temperature of 70^{o}C and boiled for 3 hours. The extractor thimble was a whatman cellulose thimble with 33mm internal and 80 mm external length. The filtrate was concentrated in an electric water bath at a temperature of about 100^{o}C for 1 hour, and was hydrolyzed with 1:2 HCl. The hydrolyzed concentrate was washed with acetone and then precipitated using ethanol as precipitating agent and was left undisturbed in the laboratory bench for 12 hours. The precipitated pectin was then separated from the precipitating solution by sieving with a muslin cloth, and dried in a hot air oven at 60 – 70^{o}C. The hard dried pectin (Figure 4) was pulverized and was sieved through a mesh. The fine orange peel pectin powder was then weighed and the percentage yield calculated, recorded and stored in air-tight container for further analysis.

Percentage yield of orange peel pectin:

$$\text{Yield (\%)} = \frac{\text{Weight of dry extracted pectin powder (g)}}{\text{Weight of dry orange peel powder (g)}} \times \frac{100}{} \text{-------- 1}$$

Figure 1. Orange fruit (*Citrus sinensis*)

Figure 2. Orange fruit peels

Figure 3. Dry peels (grinded and sieved)

Figure 4. Dry extracted pectin pellets.

Identification and confirmation of pectin:

(i) Pectin solution (sample) + Ethanol = Colorless solution
(ii) Pectin solution (sample) + NaOH = Gelatinous precipitate
(iii) Gelatinous precipitate + HCl = Colorless gelatinous precipitate

Phytochemical analysis of orange peel pectin:

Standard methods of phytochemical screening of the orange peel pectin was carried out to identify the presence of constituents such as alkaloids, flavonoids, terpenoids, saponins, tannins, anthraquinones and cardiac glycosides. The results were carefully observed and recorded.

Preparation of Erythromycin granules

Erythromycin stearate BP was used as the model drug. Wet granulation was used to prepare the erythromycin granules with various concentrations of the orange peel pectin (OPP), acacia and corn starch mucilage (CSM) as granulating agents (binders). Pulverized lactose powder was added to enhance the bulk size of the granules. The granulating agents were used at the concentrations of 2.5, 5, 7.5 and 10% w/w respectively. The prepared granules were dried in hot air oven at 55 – 60^{O}C for 1 hr, sieved and stored in a desiccator with silica gel for further analysis and compression into tablets.

Physicochemical analysis of Erythromycin granules.

Flow properties of granules

Angle of repose

The angle of repose is the angle formed by the horizontal base of the bench surface and the edge of a cone-like pile of granules. The size of the orifice was 10 mm and the height from the beginning of the funnel to end of orifice was 111 mm. The funnel was fixed in place 4 cm above the bench surface. The angle of repose (θ) was calculated as:

$$Ø = \tan^{-1} (^{h}/r) \text{ ---------- } 2$$

Where, Ø = angle of repose
h = height of cone
r = radius of the base of cone.

Bulk density

The granules (100 gm) was carefully measured and poured into a dry 250 ml measuring cylinder and the level was adjusted without compacting. The apparent volume (V_O) was read and recorded. The Bulk density was calculated in g/ml as:

$$\text{Bulk density} = {}^{M}/V_o \text{ ---------- } 3$$

Tapped density

The measuring cylinder containing the 100 gm of granules was then tapped by raising the cylinder and allowing it to drop below its own weight. It was tapped 50 times and the tapped volume (V_a) was measured. The procedure was repeated for an additional 750 tapings and again the tapped volume was measured as (V_b). If the difference between V_a and V_b was < 2%, then V_b was taken as the final tapped volume (V_f).

$$\text{Tapped density} = {}^{M}/V_f \text{ ---------- } 4$$

Where, M = weight of the sample
V_f = final tapped volume

Compressibility index

The compressibility index was calculated as:

$$\text{Compressibility index} = \frac{\text{Tapped density} - \text{bulk density}}{\text{Tapped density}} \times \frac{100}{1} \quad \ldots\ldots\ldots 5$$

Hausner's ratio

The Hausner's ratio of the granules was determined using the following formula:

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk densiy}} \quad \text{---------- 6}$$

Compression of erythromycin granules:

The granules were carefully mixed with a lubricant (1% w/w) in a tumbling mixer for 5 minutes. The blend was then compressed into tablets of 580 $\pm$ 5 mg erythromycin tablets using Manesty Single Punch Machine at 30 N/m^2 compression force. The tablets (Figure 5) were dusted and stored in airtight container for further analysis.

Evaluation of the physicochemical characteristics of erythromycin tablets

Hardness test: The hardness of the tablets was determined using the Monsanto hardness tester. From each batch, five (5) tablets were randomly selected and subjected to the test. The mean value of the 5 selected tablets was calculated and recorded in kgf.

Friability test: The friability test was determined using Erweka Friabilator. Ten (10) randomly selected tablets were carefully dusted and weighed (W_1 gm). They were then placed in the friabilator and allowed to make 100 revolution at 25 rpm. The tablets were removed and re-dusted, and weighed (W_2 gm), and the percentage weight loss was calculated from the expression:

$$\text{Friability (\%)} = \frac{W_1 - W_2}{W_1} \times \frac{100}{1} \quad \ldots\ldots\ldots\ldots\ldots 7$$

Weight variation:

Both the British Pharmacopoeia (BP) and the United States Pharmacopoeia (USP) recommended method was adopted. Twenty (20) tablets were randomly selected and weighed individually and their mean recorded. This procedure was repeated for the different formulations.

Disintegration test:

The disintegration time was determined using a Disintegration test apparatus. The apparatus consists of six separate tubes, each with an open end at the top and hold against a 10-messh screen at the bottom end of the basket rack assembly. The basket rack was then positioned in a 1 liter beaker containing 800 ml of distilled water maintained at a temperature of $37^oC \pm 2^oC$. A tablet was placed in each tube, and the basket assemblage was set to move up and down through a distance of 5.6 cm at a frequency of about 30 cycles per minute until the tablet broke down into smaller particles and pass through the mesh. The time taken was recorded and triplicate determinations were done for all the batches and their mean time (minute) recorded.

Binder efficiency:

The binder efficiency of the tablets was evaluated using tablet hardness, friability and disintegration time values. The crushing strength (Cs) – friability (Fr) ratio is given as:

$$\text{CsFr} = \frac{\text{Crushing strength (N)}}{\text{Friability (\%)}}$$

$$\text{Binder efficiency} = \frac{\text{Tablet hardness (Cs)}}{\text{Friability (Fr)}} \times \frac{1}{\text{Dt}} \quad \text{---------- 8}$$

Where, Dt = disintegration time (min)

Correlations between CsFr and Dt for the tablet formulations were determined by ANOVA and linear regression tests at $p = 0.05$, using statistical software.

***In-vitro* dissolution studies:**

In-vitro dissolution tests were carried out in triplicates using a USP dissolution apparatus (paddle) ST 7, GB Caleva Ltd, England. The apparatus contained 800 ml distilled water maintained at a temperature of $37^oC \pm 0.5^oC$ with the aid of a thermostatic control and a stirrer was kept in an outer water glass container with a heating device. The motor was then set to rotate at a speed of 120 rpm. With the aid of a 5 ml pipette, samples (5 ml) of the dissolution medium were withdrawn at every time interval of 15 min for 90 min. An equal volume of fresh medium (distilled water) at the same temperature with the dissolution medium was replaced each time withdrawal was made. The samples were filtered and suitably diluted. VU-spectrophotometer was used to measure their absorbance at maximum wavelength, $\lambda max = 285$ nm. Duplicate measurements were made and the mean values calculated and recorded.

III. Results And Discussion

Results:

Results for the phytochemical screening of *Citrus sinensis* (orange peel) powder.

The qualitative tests on the phytochemical constituents of the powdered peels showed the presence of known chemical components as per Table 1.

Table 1: Phytochemical constituents of orange peel powder

Phytochemical constituent	Result
Alkaloid	-
Anthraquinone	-
Flavonoid	+
Saponin	-
Cardiac glycoside	-
Terpenoid	-
Tannin	-
Carbohydrate	+
Reducing sugar	+

KEY: + Positive - Absent

Results of the organoleptic properties and the yield are shown in Table 2.

Table 2: Yield and organoleptic properties of orange peel pectin powder

Parameter	Result
Colour	Greenish yellow
Odour	Characteristic
Nature	Amorphous
Solubility	Soluble in water, insoluble in acetone
pH	6.36 $\pm$ 0.76
Taste	Bitter
% Yield	10.3 (cheesecloth)

The percentage yield of the orange peel pectin extract was 10.3. According to Enkuahone (2018), the yield of orange peel pectin among other factors depend on the retrieval methods of the precipitated pectin. He found the pectin yield for the centrifugation and cheesecloth methods to be 14.3% and 10.6% respectively. The pectin yield from this present study 10.3% reasonably agree with the above reports.

Table 3: Physiochemical properties of Erythromyin granules

Formulation (% w/v)		Angle of repose	Bulk density (g/cc)	Tapped density (g/cc)	Compressibility index (%)	Hausner's ratio	Flow rate (g/cc)
Acacia	2.5	21.2	0.56	0.64	13.36	1.52	0.50
Acacia	5.0	20.5	0.50	0.55	9.48	1.10	0.41
Acacia	7.5	19.7	0.50	0.65	22.88	1.29	0.63
Acacia	10.0	25.9	0.52	0.56	10.00	1.11	0.67
CSM	2.5	27.6	0.56	0.59	3.26	1.05	0.77
CSM	5.0	20.5	0.50	0.59	8.82	1.17	0.34
CSM	7.5	27.4	0.53	0.65	11.88	1.22	0.71
CSM	10.0	28.6	0.56	0.64	8.54	1.15	0.67
OPP	2.5	27.5	0.43	0.50	7.45	1.18	0.83
OPP	5.0	30.9	0.40	0.48	16.00	1.10	1.11
OPP	7.5	30.6	0.48	0.59	19.04	1.23	1.00
OPP	10.0	30.2	0.43	0.49	10.86	1.12	0.83

Table 4: Mean and standard deviation of the physiochemical properties of Erythromycin granules

Parameter	Acacia	CSM	OPP
Angle of repose (^{O})	20.57 $\pm$ 4.59	20.07 $\pm$ 3.74	9.82 $\pm$ 1.51
Bulk density (g/cc)	0.51 $\pm$ 0.02	0.53 $\pm$ 0.02	0.43 $\pm$ 0.03
Tapped density (g/cc)	0.59 $\pm$ 0.05	0.61 $\pm$ 0.03	0.51 $\pm$ 0.05
Compressibility index (%)	13.93 $\pm$ 6.20	8.12 $\pm$ 3.57	13.33 $\pm$ 5.12
Hausner's ratio	1.25 $\pm$ 0.19	1.14 $\pm$ 0.07	1.15 $\pm$ 0.05
Flow rate (g/cc)	0.55 $\pm$ 0.11	0.62 $\pm$ 0.19	0.94 $\pm$ 0.13

CSM = Corn starch mucilage; OPP = Orange peel pectin

The data from Table 4, show that the granules of different formulations had good flow characteristics, thereby indicating good compressibility.

Table 5: Physiochemical properties of erythromycin tablets formulated with different types and concentration of binders

Formulation binder (% w/v)		Weight variation (mg)	Hardness (kg/cm^3)	Friability (%)	Disintegration time (min)	Binder efficiency
Acacia	2.5	581 ± 0.04	4.6 ± 1.5	0.75 ± 0.02	6.91 ± 0.7	0.887
Acacia	5.0	580 ± 0.01	4.8 ± 0.8	0.70 ± 0.10	9.5 ± 0.04	0.722
Acacia	7.5	579 ± 0.02	5.4 ± 1.01	0.60 ± 0.11	14.5 ± 0.11	0.621
Acacia	10.0	582 ± 0.01	6.1 ± 0.05	0.40 ± 0.12	20.1 ± 0.02	0.759
CSM	2.5	580 ± 0.03	4.4 ± 0.02	0.91 ± 0.10	6.5 ± 0.05	0.744
CSM	5.0	581 ± 0.04	4.8 ± 1.01	0.85 ± 0.02	10.2 ± 0.10	0.554
CSM	7.5	578 ± 0.06	5.6 ± 0.08	0.70 ± 0.02	15.0 ± 0.20	0.533
CSM	10.0	582 ± 0.02	6.4 ± 0.03	0.45 ± 0.03	21.4 ± 0.03	0.665
OPP	2.5	580 ± 0.01	4.5 ± 0.02	0.75 ± 0.14	7.5 ± 0.04	0.800
OPP	5.0	580 ± 0.04	4.7 ± 0.4	0.72 ± 0.10	10.3 ± 0.01	0.634
OPP	7.5	579 ± 0.01	5.4 ± 1.02	0.60 ± 0.03	15.2 ± 0.04	0.556
OPP	10.0	580 ± 0.03	6.7 ± 0.05	0.41 ± 0.04	25.4 ± 0.05	0.643

CSM - Corn starch mucilage; OPP = Orange peel pectin

The physicochemical characteristics of the various formulations of erythromycin tablets are shown in Table 5. For acacia 2.5 – 10% w/v, the weights varied from 579 ± 0.02 mg to 582 ± 0.01 mg; CSM 2.5 – 10% w/v, weights varied from 578 ± 0.06 mg to 582 ± 0.02 mg and OPP 2.5 – 10% w/v, the weights varied from 570 ± 0.01 mg to 580 ± 0.01 mg respectively. The various formulations pass the weight uniformity test as the percentage deviation falls within 5% for tablets greater than 250 mg as specified by the British Pharmacopoeia (BP). The hardness (kgf) of all the tablet formulations ranged from 4.4 ± 0.02 to 6.7 ± 0.05 (kgf) respectively. The British Pharmacopoeia specifies that the hardness of tablets with values ≥ 4 are acceptable so long as the disintegration time are not affected from Table 5 and Figure 6, it is seen that the hardness increased with increase in binder concentration. Their friability (%) also varied from 0.04 ± 0.12 to 0.91 ± 0.01 % respectively. The BP specifies a maximum limit of 1% friability; hence as shown in Table 5, all the formulations pass the friability test. The % friability however, decreased with increase in the binder concentrations (Figure 7). Also, the disintegration time values range from 6.91 ± 0.7 to 20.1 ± 0.02 (min) for Acacia 2.5 – 10% w/v; 6.5 ± 0.05 to 21.4 ± 0.03 (min) for CSM 2.5 – 10% w/v; and 7.5 ± 0.04 to 25.4 ± 0.05 (min) for OPP 2.5 – 10% w/v respectively. The Erythromycin tablets formulated with the different types and binder concentration 2.5 – 7.5% w/v, pass the disintegration time test for conventional tablets of not more than 15 minutes. However, tablets formulated with 10% w/v of the 3 types of binders only disintegrated at 20.1 ± 0.02 (min (Acacia); 21.4 ± 0.03 (min) (CSM) and 25.4 ± 0.05 min (OPP) respectively. Generally, the disintegration time increased with increase in binder concentration (Figure 8).

The binder efficiency is a measure of the interaction between tablet hardness, friability and disintegration time. A higher binder efficiency, implies that tablets formulated with it possess excellent hardness, low friability (≤ 1%) and short disintegration time (Alabiowu *et al*., 2009; Lawal et al., 2015). From the values obtained in Table 5, the binder efficiency were high for all the formulations which indicate good binding property of the batches formulated.

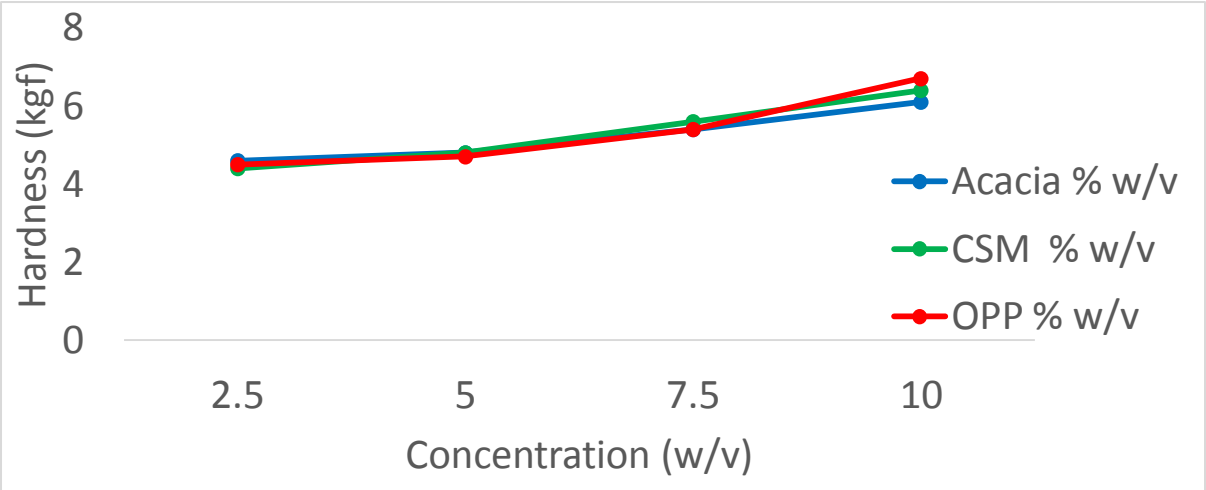

Figure 5. Relationship of binder concentration versus hardness of erythromycin tablet

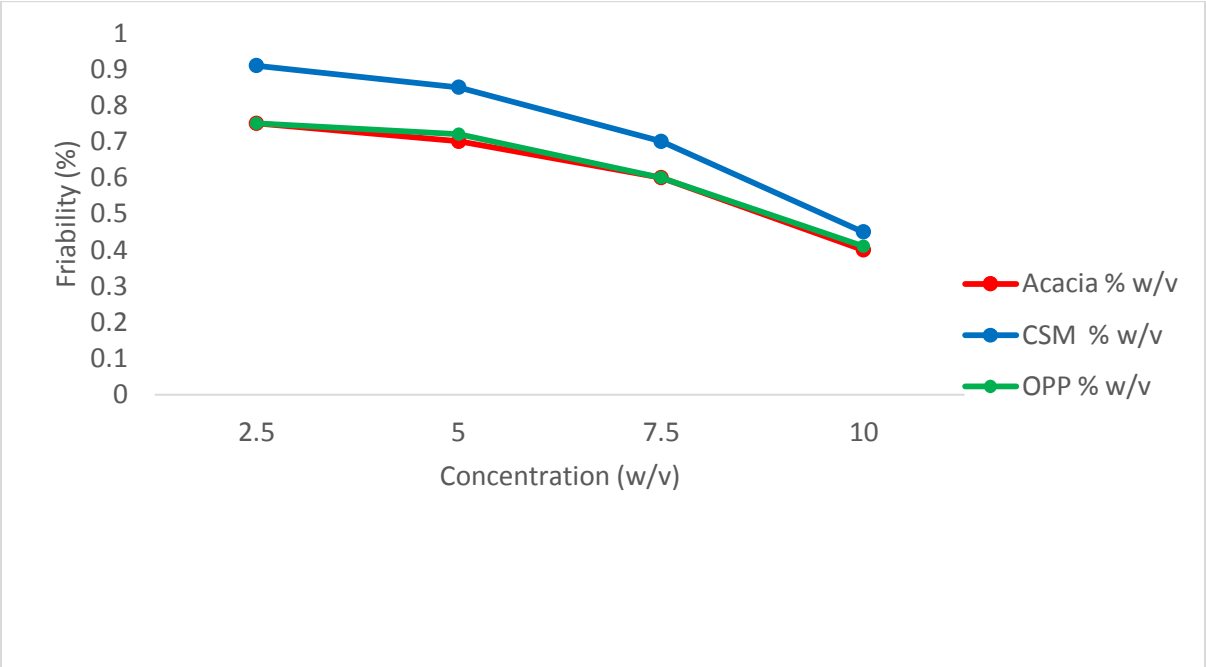

Figure 6. Relationship of binder concentration versus friability of erythromycin tablet

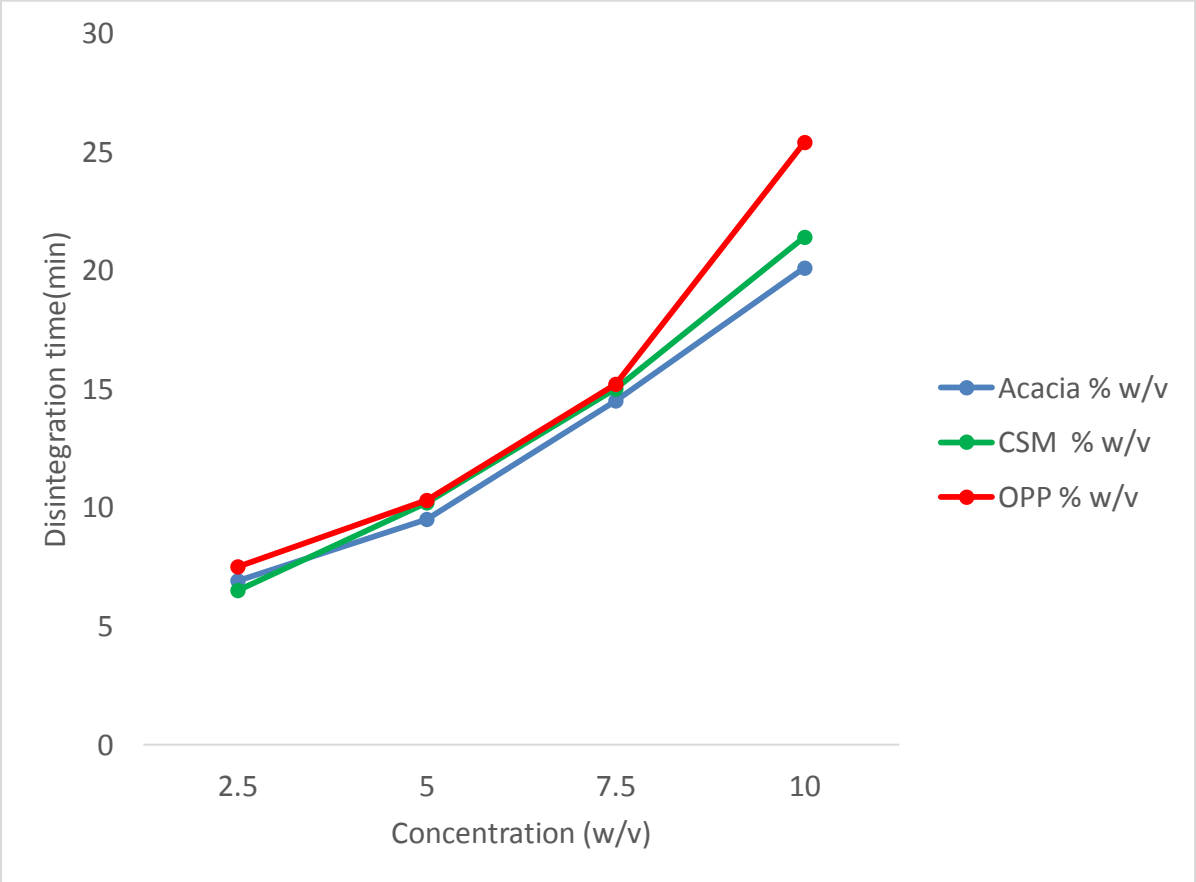

Figure 7. Relationship of binder concentration versus disintegration time of erythromycin tablet

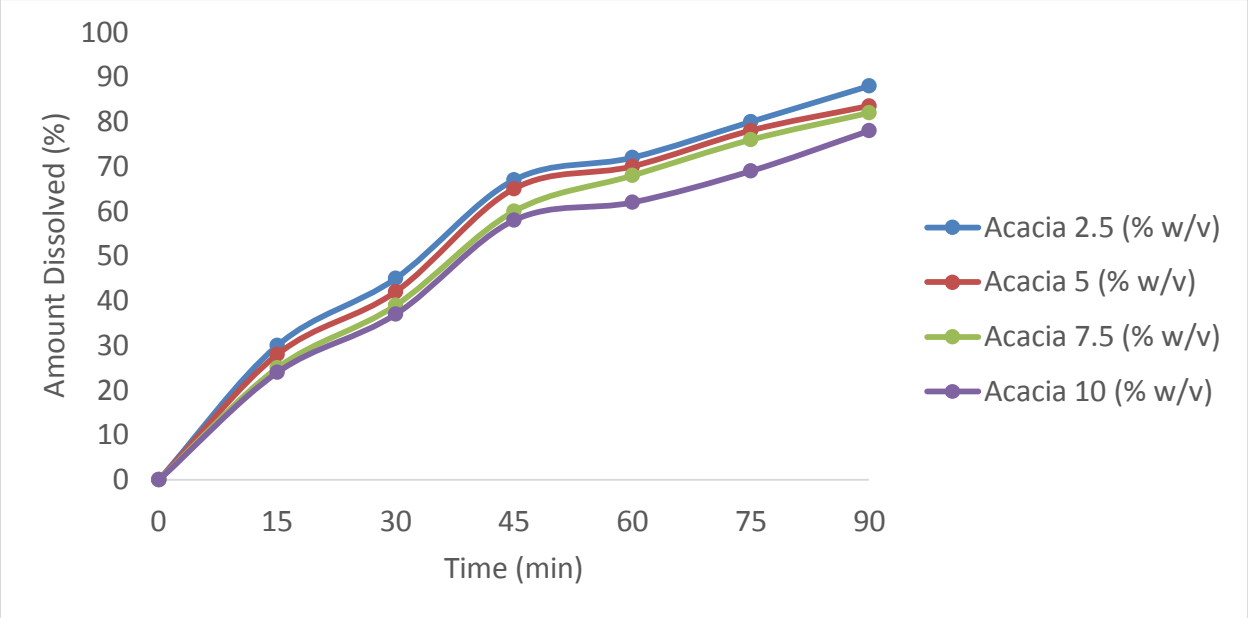

Figure 8. Dissolution profile of erythromycin tablet formulated with varying conc. of acacia.

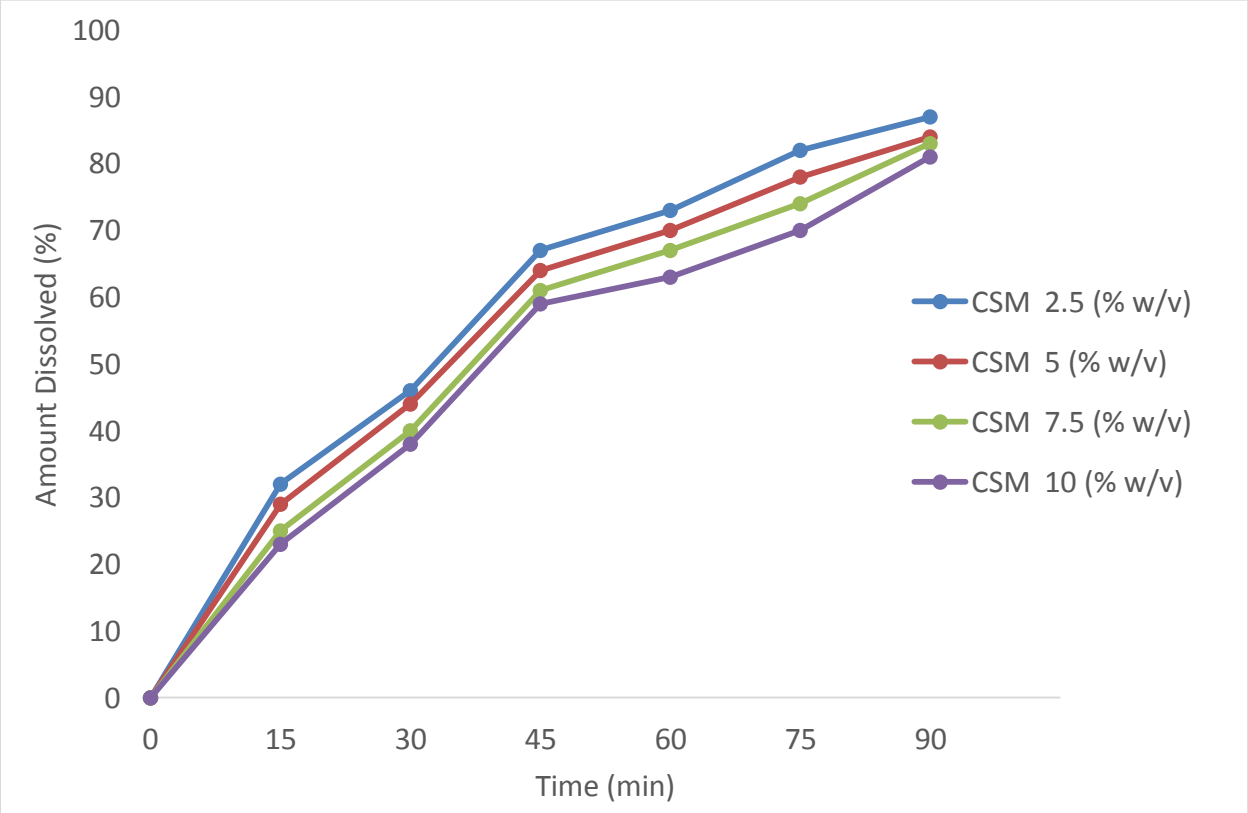

Figure 9. Dissolution profile of erythromycin tablet formulated with varying conc. of corn starch mucilage (CSM).

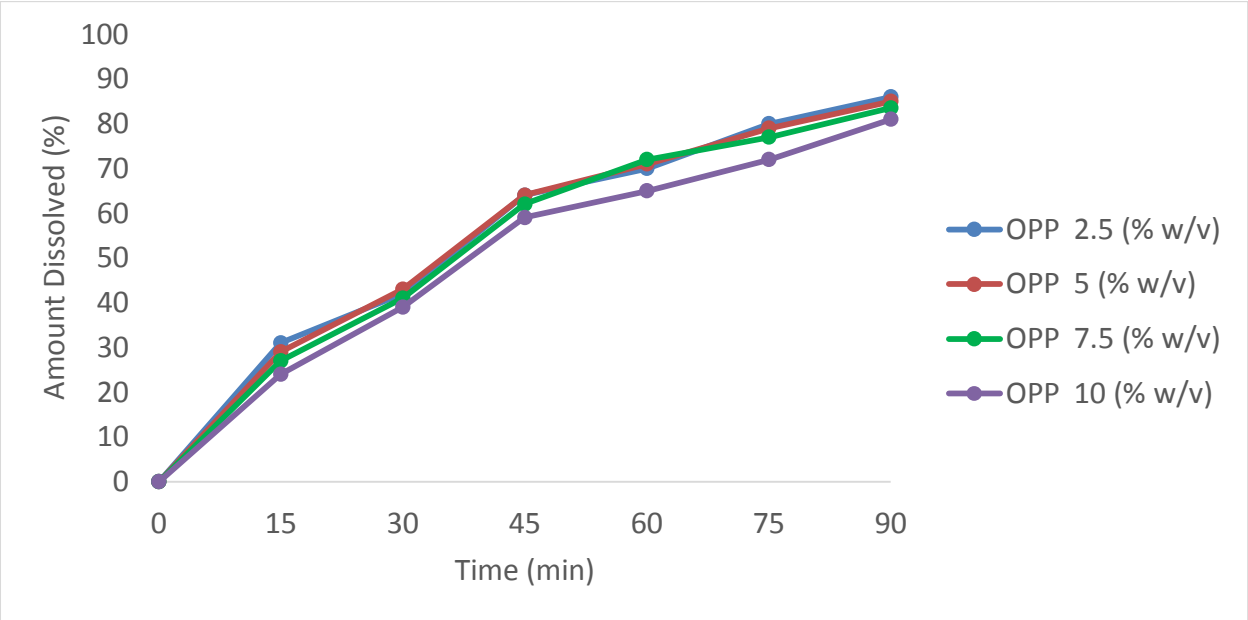

Figure 10. Dissolution profile of erythromycin tablet formulated with varying conc. of orange peel pectin.

Table 6: Dissolution parameters of Erythromycin tablets

Batches	M∞ (%)	t∞ (min)	M∞/t∞ (% min)
BF1 (Acacia)	84.50	90	0.939
BF2 (CSM)	83.75	90	0.931
BF3 (OPP)	83.50	90	0.928

Table 7: Regression coefficient values for different release models

Formulations	Zero order	First order	Higuchi model	Korsmeyer-peppas model	Hixson-Crowell model
	R^2	R^2	R^2	R^2	R^2
BF1 (Acacia)	0.924	0.945	0.987	0.892	0.886
BF2 (CSM)	0.902	0.956	0.982	0.885	0.840
BF3 (OPP)	0.913	0.960	0.991	0.896	0.895

Release kinetics and mechanism of drug release from the erythromycin tablets.

Table 7 shows the results of the various release kinetics for erythromycin tablets formulated with the three different binders. The results from the dissolution studies were fitted into zero order, first order, Higuchi, Korsmayer-peppas and Hixson-Crowell release models to determine the release kinetics of the different formulations. The in-vitro release profiles of the erythromycin tablets simulated the Higuchi release model as the plot showed the highest regression coefficient (R^2) values of 0.982 – 0.991 compared to the zero, and first order release models which had values form 0.902 – 0.924 and 0.945 – 0.960 respectively. For Korsmeyer-peppas and Hixson-Crowell models, the regression coefficient values were 0.885 – 0.896 and 0.840 – 0.895 respectively. The results show that the drug released from the tablets were mainly by Higuchi's model, which states that the amount of drug released is dependent on the square root of time dependent process based on Fickian diffusion equation (Thakur et al., 2016; D.R. Paul (2010); Airemwen C.O. et al., 2020). The results obtained were found to be in agreement with the studies conducted by Higuchi, 1963. In the study he analyzed the mechanism of drug release from matrices and postulated two mechanisms which are dissolution and diffusion controlled mechanisms (Higuchi T, 1963).

IV. Conclusion

Biodegradable materials derived from agricultural wastes are currently being converted to wealth in the pharmaceutical industries as excipients in pharmaceutical dosage forms, and also in food and allied industries for various functions as adjuvants and as suspending agents. Orange peel wastes are numerous and could constitute environmental nuisance. Pectin which is widely used in the preparation of some pharmaceutical dosage forms, in the food and paint industries as thickners can be derived in commercial amounts from this natural plant source – orange peel (citrus sinensis). The results from this research work has demonstrated that orange peel pectin can be employed as a binder substitute in erythromycin tablet formulationas.

References

[1]. Aina VO; Barau MM; Mamman OA; Zakari A; Haruna H; Umar MSH; Abba YB (2012). "Extraction and characterization of pectin from peels of lemon (*Citrus lemon*), grape fruit (*Citrus paradisi*) and sweet orange (*Citrus sinensis*)." British Journal of Pharmacology and Toxicology, 3(6), 259 – 262.

[2]. Airemwen CO, Olarinoye AA and Uhumwangho MU (2020). Effects of sodium chloride as channeling agent on release profile of diclofenac tablets formulated using Grewia mollis and acacia gums. *J. Pharm and Allied Sci*, 17(1): 3203 – 3209.

[3]. Alebiowu G, Adebolu AA (2009). Disintegrant properties of paracetamol tablet formulation lubricated with co-processed lubricants. *Formacia*, 57:500-510.

[4]. Enkuahone Abebe Alamineh (2018). Extraction of Pectin from orange peels and characterizing its physical and chemical properties. *American Journal of Applied Chemistry*, Vol. 6, No. 2, pp 51-56, doi:10.11648/j.agac.20180602.13.

[5]. Erythromycin: The American Society of Health System Pharmacists. Archived from the original on 2015-09-06, Retrieved May 12th 2021.

[6]. FAO Satistics, 2018 – Food and Agriculture Organization of the United Nations.

[7]. Femi-Oyewo MN, Adedokun Oluseun M, Olusola TO (2004). Evaluation of the Suspending Properies of *Albizia Zygi*a gum on Sulphadimidine Suspension, *Tropical Journal of Pharmaceutical Research*. 3(1): 279-284

[8]. Higuchi T (1963). Mechanism of sustained action medication: Theoretical analysis of rate of release of soil drugs dispersed in solid matrices. *J. Pharma Sci,* 52: 1145-1149.

[9]. Kulkarni GT, Gowthamarajan K, Dhobe FY, Suresh B (2005). Development of Controlled release spheroids using natural polysaccharide as release modifier, *Drug Deliv*, 12: 201 -206

[10]. Lawal MW, Odeniyi MA, Itiola OA (2015). Effects of thermal and chemical modifications on the mechanical and tablet formulations containing corn, cassava, and sweet potato starches as filler binders. *Asian Pacific Journal of Tropical Biomedicine;* 5:585-590.

[11]. M. Ravindrakullai Reddy, Kopparam Manjunath (2013). Evaluation of petin derived from orange peel as a pharmaceutical excipient. *Int. Journal of drug Development and Research*, 5(2): 283 – 294.

[12]. Mitul T. Pasel, Jitendra K. Patel and Umesh M. Upadhay (2012). Assessment of varius pharmaceutical excipient properties of natural moringa oleiferagum (Mucoadhesion disintegration, binder). *International Journal of Pharmacy and Life Sciences*, Vol. 3, Issue 7: 1833-1847. ISSN: 0976-7126.

[13]. Morton J. 1987. Orange: p.134-142. In: Fruits of warm climates. Julia F. Morton, Miami, FL. Assessed May 12th, 2021.

[14]. Paul DR (2010). Elaborations on the Higuchi model for drug delivery. *International Journal of Pharmaceutics*, 418(1): 13-17.

[15]. Shekhar Pandhari Pande and Harshal Makode (2012). Separation of oil and pectin from orange peel and study of effect of pH of extracting medium on the yield of pectin. *Journal of Engineering Research and Studies*; 3(2): 1 – 4. E-ISSN0976-7916.

[16]. Thakur G., Singh A, Singh I (2016). Chitosan-Montmor-illonite polymer composites; formulation and evaluation of sustained released tablets of aceclofenac. *Sci. Pharm.* 84: 603 – 618.

[17]. Tiwari A, Aggarwal A, Tang W, Drewnowski A (2017). Cooking at Home: A Strategy to comply with U.S. Dietary Guidelines at No Extra Cost, *Am J Prev Med*, pii: SO749-3797(17) 30023-5

[18]. Tobias I, Ndubuisi Ezejiofor, N.V. Eke, R.I. Okechukwu, R.N. Nwoguikpe and C.M. Duru (2017). Waste to wealth: Industrial raw materials potential of peels of Nigerian sweet orange (citrus sinensis). *African Journal of Biotechnology*, Vol 10 (33), pp. 6257 – 6264.

[19]. Tushar S, Zia UM, Shadhan KM, Md. Sakhawat H, Md. Abu J, Rafigul IS, Titumeer F (2018). Application of Natural Polymers as Pharmaceutical Excipients, *Global J Life Sci Biol Res* 4:1 doi: 10. 24105/gjlsbr. 2018.4.2

[20]. Xu, Q, Chen, LL, Ruan x, (2013). The draft genome of sweet orange (citrus sinesis). *Nature Genetics*, 45, 59-66. https://doi.org.10. 038/ng.2472.

OBARISIAGBON, et. al. "Citrus Sinensis Peel Pectin: A Novel Binder in Erythromycin Tablet Formulation." *IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS)*, 17(1), (2022): pp. 51-60.