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In vitro evaluation of erythromycin incorporated with β-cyclodextrin and povidone polymers for capsule drug delivery

Nnabuike D Nnamani[1*];Ph.D, Emokpae George[1];B.Pharm, Alonge Taye Abimbola[1];B.Pharm, Nathaniel Ejike Oyenwe[2];Ph.D

[1]Department of Pharmaceutics and Pharmaceutical Technology, College of Pharmacy, Igbinedion University, Okada, Edo State, Nigeria.
[2]Department of Pharmaceutical Microbiology, College of Pharmacy, Igbinedion University, Okada, Edo State, Nigeria.

Abstract

Entrapment of drugs within polymers have been used to modify dosage drug release. The aim of this work is to compare the entrapment potentials of water soluble povidone and or β-cyclodextrin polymers in encapsulated erythromycin. Drug-polymer interaction was determined using FTIR, SEM and DSC. Using 23 factorial design, 8 variant polymer combinations were devised. Wetted erythromycin and polymer mix was kneaded and granulated. The granules were dried and analysed for drug-loading and micromeritic properties before being filled into a hard gelatin capsule. The capsules were analysed for physicochemical and antimicrobial properties. The FTIR spectrum of the drug-polymer depicts the leading peaks of erythromycin. SEM images and DSC thermogram of the drug-polymers showed irregular fluffy and porous structures, and reduction in endothermic temperatures respectively. The granules showed Carr's index, Hausner ratios and angle of repose < 24.07, 1.31 and 30.51° respectively, and over 97.81 % drug entrapment. All capsules met USP specification for weight uniformity. Erythromycin-povidone capsules disintegrated within 15 min, had 53 % dissolution in 15 min, and 53 – 100 % dissolution within 180 min. At 25 mg/ ml, erythromycin-povidone capsule gave zones of inhibition of 37.67 – 39.83 mm. FTIR analysis of the erythromycin-polymer mix indicated compatibility of erythromycin with the polymers, the SEM indicated formation of amorphous complex, while the DSC inferred non-complex interaction and improvement in solubility. In comparison with formulations with erythromycin-β cyclodextrin complex, erythromycin-povidone complex showed better promise in enhancing erythromycin capsule formulation and antimicrobial properties.

Keywords: Entrapment, wet granulation, kneaded, antimicrobial.

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1. Introduction

Advances in material science and chemical engineering allow for modification of particle size, shape, surface characteristics, and other factors affecting the functional properties of conventional and new drugs (1). Techniques such as drug-polymer attachment can modify drug release, target site of drug action and protect drug from conditions such degrading pH, enzyme and other trigger stimuli (2-4). Drug-polymer attachments have been prepared using techniques such as physical blending and kneading (5, 6). The technique and type of polymer such as water soluble

Corresponding Author: Nnabuike D Nnamani, Department of Pharmaceutics and Pharmaceutical Technology, College of Pharmacy, Igbinedion University, Okada, Edo State, Nigeria.
Email address: nnamani.didacus@iuokada.edu.ng

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β-cyclodextrin and povidone, used can have varied drug delivery effects (5). β-cyclodextrin is one of the major cyclodextrin obtained from modified starch (7). It is a ringed, cyclic, hollow and truncated oligosaccharide that can form hydrophobic cavities in aqueous medium. Modulation of pore activity and sensing of β-cyclodextrin can modify and target drug delivery (8). Povidone is the water soluble and biodegradable polyvinylpyrrolidone polymer used for different applications in solid, semi-solid and liquid pharmaceutical preparations (5, 7, 9-11).

Erythromycin was chosen as the model drug to study the effect of water soluble polymer on drug activity. Erythromycin is a wide spectrum antibiotic used in treatment of infections from gram negative and positive pathogens such as Staphylococcus sp (12, 13). Erythromycin is bitter tasting, very hydrophobic, practically insoluble in water and sparingly soluble in aqueous buffers and stable at pH 7 and 8 (12-14). Researchers such as Platon *et al*. (12), Kempe *et al*. (13), Cyphert *et al.* (14) and Yu *et al*. (15) have demonstrated that complexing erythromycin inside a water-soluble polymer can mask its bitter taste, protect it from gastric acidic degradation, and improve its contact with and solubility in water.

Some research has revealed that physical engineering that improves solubility and modify delivery properties may reduce therapeutic efficacy of some drugs (16-19). This revelation suggests that evaluation of drug complexes should extend beyond physicochemical determinations to bioassay and patient based tests. The aim of the research work is to compare the effect of β-cyclodextrin and povidone polymers in the formulation of erythromycin granules by first using Fourier Transform Infrared Spectroscopy (FTIR) and Differential Scanning Calorimetry (DSC) to determine the pharmaceutical compatibility and characterisation of the polymers with the active drug, and then formulate erythromycin granules using the polymers, determine the antimicrobial activities of the conjugated and free erythromycin granules and characterize the physicochemical and antimicrobial properties of the granules that relate to its use in capsule formulation and drug delivery.

2. Material and methods

2.1. Materials

Erythromycin (Kermel), Povidone (Kermel), β-cyclodextrin (Macklin), microcrystalline cellulose Avicel PH-102 (Salt Minerals GmbH, Korbach, Germany), lactose (Sigma Chemicals, St. Louis, USA), magnesium stearate (A.H.A. International Co. Ltd, China), hard gelatin capsules and antimicrobial susceptibility discs (Thermo Fisher Scientific, Massachusetts, US) were gifted by Ulticare-lyka Pharmaceutical Nigeria Limited. Staphylococcus sp. was obtained from human clinical isolates at the University of Benin Teaching Hospital and processed at the Pharmaceutical Microbiology Laboratory in Igbinedion University Okada.

2.2. Design of formula and pre-formulation of powders

Povidone, β-Cyclodextrin, and starch were used as variants in 23 factorial design to draft the formula for batches A – H presented in Table 1. Preparatory to formulation, 25 g erythromycin powder, 15 g β-Cyclodextrin, 15 g povidone, and 50 g starch powders were separately weighed out, pulverised, passed through sieve size 0.75mm and kept. A 2 g drug-polymer blend was analysed for interaction and compatibility.

2.3. Pre-formulation characterization and compatibility studies

2.3.1. Differential Scanning Calorimetry (DSC) analysis

A 5.2 mg samples of povidone, β-cyclodextrin, 1:1 dispersions of erythromycin in povidone or 1:1 dispersions of erythromycin in β-cyclodextrin polymers was analysed using a PerkinElmer Differential Scanning Calorimeter (Model DSC 800, PerkinElmer Private Limited, India) adapting the method of Talik *et al*. (20). The calorimeter (Model DSC 800, PerkinElmer Private Limited, India) was operated at a heating rate of 10 °C per minute from 0 - 250 °C applied under nitrogen purging at 20 ml / min. A sample was put inside the samples were placed in a sealed aluminium pan cuvette with a pierced lid of the calorimeter with the left and right limits set to 30 and 160 °C respectively, and read of using the universal analysis software version 4.5A of the attached monitor. Readings and the thermogram curve was obtained and analysed.

2.3.2. Fourier transmission infrared radiation (FT-IR)

A 2mg sample povidone, β-cyclodextrin and combination of povidone and β-cyclodextrin polymers, erythromycin or 1:1 dispersions of erythromycin in the different polymers was weighed and made up to 200 mg with KBr. The mixture was blended, pulverised and dried at 110 °C for 2 hours in a hot air oven. The dried mixture was compressed to 80 mg pellets using a 13 mm diameter die and 8 tons of pressure for 3 minutes. FT-IR spectrum was recorded using Schimadzu FT-IR-8400S Fourier transmission infrared spectrophotometer. All readings were taken at a scan range of 4000-650/cm with resolution of 4/cm and 16 / cm and recorded.

2.3.3. Scanning electron microscopy (SEM)

SEM analysis was conducted by sprinkling a sample onto a double-sided adhesive carbon conductive tape which was mounted on a microscopic stub of copper. The tapes were then sputter-coated with gold using an ion sputtering device of the equipment. The SEM images of the samples were taken at an acceleration voltage of 20 kv at various magnifications.

2.4 Preparation of granules

Using the formula in Table 1, polymer, avicel or blend was dispersed in 2 ml water and the dispersion was milled for 10 min using Kenwood Multi-mill tube mill (Kenwood Corporation, Hachiji, Tokyo, Japan). Adapting the method of Brtel *et al.* (21) for kneading, erythromycin was wetted with 2 ml 50 % ethanol in a beaker and mixed using a glass rod. The wet erythromycin and the milled dispersion were poured into a glass mortar, mixed thoroughly and kneaded to semi-solid lumps. The lumps were passed through 1.2 mm stainless steel sieve` to produce wet granules. The wet granules were dried in a hot air oven (Model DHG-9053A, Ocean Medical, England) for 10 min at 70 °C. The semi-dried mass was removed from the oven, kneaded, sieved through the 1.2 mm stainless steel sieve, and dried in the oven for 20 min at 70 °C. The dried granules were allowed to cool for 20 min and gently mixed with magnesium stearate and talc, and stored in a desiccator awaiting analysis and filling into hard gelatin capsule shells.

2.5. Evaluation of granules

Granules were evaluated for micromeritics properties of Hausner ratio, Carrs' index, angle of repose and flow rate, and for drug loading and drug entrapment properties.

2.5.1. Hausner ratio and Carrs' index

Hausner ratio and Carr's index of granules was determined by pouring 5 g of test granules through a funnel into a 50 ml glass cylinder. The cylinder was gently tapped three times, and the volume of the granules read and recorded as the bulk volume. The cylinder was allowed to drop on the flat surface on a padded table from 5 cm height. The volume occupied by the granules after 1000 drops was read and recorded as the tapped volume. The bulk and tapped densities of the granules were derived by dividing their respective bulk and tapped volumes by 5 (the weight of granule). The tapped density divided by the bulk density was calculated as the Hausner ratio. The difference

Table 1. Formula for Producing 10 Erythromycin (250 mg) Inclusion Complex Capsule

	(g)							
	A	B	C	D	E	F	G	H
Erythromycin	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
β-cyclodextrin	2.5	2.5	2.5	2.5	0	0	0	0
Povidone	2.5	0	2.5	0	2.5	0	2.5	0
Avicel	0.5	0	0	0.5	0.5	0.5	0	0
Starch	2.0	5	2.5	4.5	4.5	7.0	5	7.5
Magnessium stearate	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
Talc	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
Total	10.02	10.02	10.02	10.02	10.02	10.02	10.02	10.02

NB: Each capsule of 500 mg granules contains 250 mg erythromycin active ingredient.

of the tapped density and bulk density divided by the tapped density was calculated as Carr's index.

2.5.2. Angle of repose

Angle of repose of granules was determined by pouring 5 g granules through a funnel, clammed to a retort stand at 10 cm from base, to form a heap. The base and the height of the heap formed were measured and recorded. The angle the heap made with base (angle of repose) was calculated from the arc-Tan of the result of height of heap divided by half of the base of heap.

2.5.3. Flow rate

Flow rate of granules was determined using a retort stand clamped to a funnel placed 10 cm from a flat base. With the end of the funnel covered, 5 g granules were poured into the funnel. Using a stopwatch timer, the covered end of the funnel was removed, and the time taken for all the granules to pass through recorded. The test was repeated in triplicate, and the average time of fall of the granules used to divide the 5 g granules to get the flow-rate of the granules.

2.5.4. Drug-loading and drug entrapment efficacy

Drug-loading and drug entrapment efficacy was determined by transferring 500 mg granules into a 100 ml volumetric flask of a probe sonicator (PCI Analytics, Mumbai, India) and made up to volume with acidified methanol. The sonicator was operated for 2 min and the dispersion formed, filtered and analysed for erythromycin using a UV-visible spectrophotometer (Model 23D, Uniscope, England) at 285 nm wavelength (λmax). The drug entrapment efficacy were calculated from equations 1 below;

$$\textit{Drug entrapment efficacy} = \frac{\textit{actual drug in granules}}{\textit{theoretical drug in load}} \quad \text{(Eq. 1)}$$

2.6 Filling of granules into capsules

A size 00 hard gelatin capsule shell was separated by splitting the head from the body. A 500 mg erythromycin granules, containing 250 mg erythromycin active, was filled into the opened capsule shell, covered and sealed tight with the cap. The filled capsule was stored in a dry bottle container, and appropriately labelled.

2.7. Evaluation of capsules

2.7.1. Weight uniformity

Capsule weight uniformity test was conducted on 20 capsules. The weight of empty size 00 hard gelatin capsule was taken. From each batch, 20 capsules were randomly chosen and weighed both individually and collectively (less the weight of the hard gelatin capsule, and the mean weight was also computed.

2.7.2. Disintegration time

Disintegration time test for capsule was conducted on six randomly selected capsules using disintegration tester (DT) (MK4, Manesty Machine Limited, England) operated at 30 cycles / mm in a disintegration medium of 1000 ml of 0.1 N HCl at a temperature of 37 ℃. Each one of the six capsules were placed in one of the six-opened cylindrical transparent tubes of the basket-rack assembly of the tester, operated and observed over 30 min. The time taken for each capsule to completely disintegrate was recorded and used to get the average disintegration time of the six capsules. The test was repeated three times, and the average result recorded.

2.7.3. Dissolution rate

Dissolution rate test was carried out on capsules using the basket method. A capsule was placed in a basket immersed in 900 ml of 0.1 N HCl dissolution fluid maintained at 37±2 °C and operated for 2 hr at 50 rpm, and the dissolution medium was replaced with phosphate buffer solution of pH 6.8 for the remaining 6 hr. At 15, 30, 45, 60, 90, 120, 150 and 180 minutes intervals, 5 ml samples of the leaching fluid were withdrawn with a pipette fitted with cotton wool filter, and replaced with 5 ml dissolution fluid. The withdrawn fluid was diluted 1:100, and the absorbance determined with UV- spectrophotometer (Model 23D, Uniscope, England) at a wavelength (λmax) of 285 nm. The test was repeated in triplicates for each batch. The concentration of drug release was calculated from the absorbance using the standard calibration of the pure erythromycin powder. The percentage erythromycin released from the formulation concentration was calculated.

2.7.4 Antimicrobial susceptibility

Antimicrobial properties of the capsules

were determined by adapting the Kirby-Bauer antibiotic sensitivity test method of Morello *et al.* and Barnes *et al.* (22, 23 wq). Bacteria specimens obtained from Igbinedion University Teaching Hospital were cultured in a sterile blood agar plate and incubated for 24 h at 37 °C. The discrete colonies obtained were further inoculated into a sterile mannitol salt agar plate and incubated for 24 h at 37 °C. The colonies with 1-2 mm in diameter, round, raised and opaque, characteristic of Staphylococcus sp. were subjected to gram stain test. Colonies that appeared as Gram-positive cocci with irregular grape-like clusters were further isolated as *Staphylococcus* sp.. Identified isolates from a Staphylococcus sp. colony was dispersed in water to 0.5 Mcfarland suspension turbidity standard. A loopful from the suspension was placed and inoculated in a pure culture nutrient broth suspension for 24 h. Using a 2 ml syringe, 1 ml of pure culture suspension was diluted with 9 ml distilled water. The 10 fold serial dilution was applied to get a 10-4 concentration. A 0.2 ml of the 10-4 dilution was taken with a syringe, inoculated and spread evenly with a sterile rod over the surface of the sterile Mueller-Hinton agar plate. A 500 mg granules, equivalent to 250 mg erythromycin, from a test capsule or 250 mg pure erythromycin was dispersed 1000 ml of deionized water at 37 °C, stirred using a magnetic stirrer and filtered. The filtrate was further diluted with water to get 25, 12.5, 6.25, 3.13, and 1.57 µg / ml erythromycin solutions. Sterile filter paper disc was placed inside a solution and allowed to be soaked and impregnated for 10 min. With the aid of sterile forceps the impregnated disc was placed in the centre of swabbed Mueller-Hinton agar plate. The plate was inverted and incubated for 24 h at 37 °C in the candle extinction jar. The microbial growth was observed and the result of the zones of inhibition recorded. The tests were conducted in triplicates for all batches.

2.8 Statistical Analysis

The result data were expressed as mean and standard deviation (mean ± SD) and their significant differences were determined using Student's t-test. Differences were considered significant at P values <0.05 or not significance: n.s.

3. Results and discussion

3.1 Pre-formulation

3.1.1 DSC thermogram

The DSC analysis results for erythromycin, polymers and drug-polymer blend are presented in figure 1. The first endothermic peaks for erythromycin-povidone and erythromycin-β-cyclodextrin complexes were observed at 65.05 and 64.98 °C respectively, and can be attributed

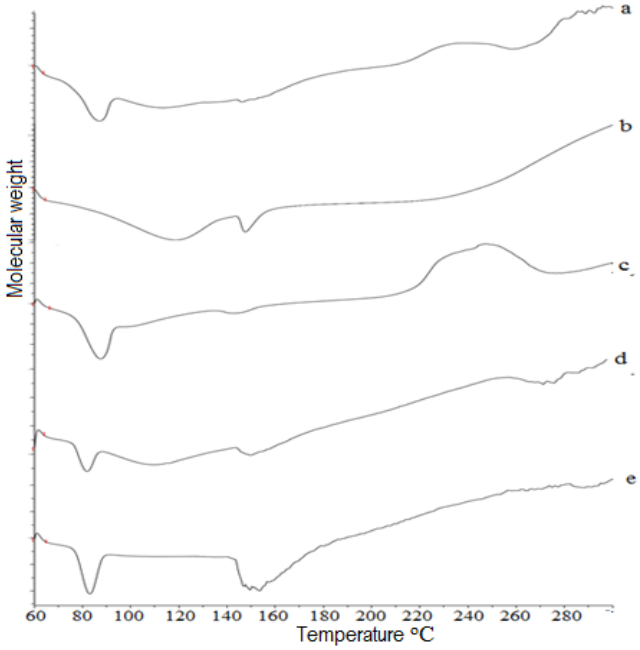

Figure 1. Differential Scanning Calorimetry Thermogram Curve .
Key: a = povidone, b = β-cyclodextrin, c = erythtomycin, d = povidone-erythromycin blend, e = β-cyclodextrin - erythromycin blend.

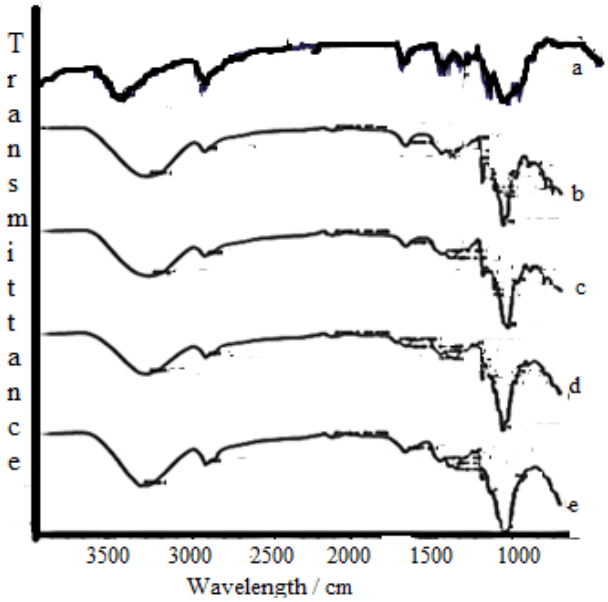

Figure 2. FTIR spectrum for powders.
Key: a = erythromycin, b = β-cyclodextrin, c = Povidone, d = erythromycing – β-cyclodextrin blend, e = erythromycin – povidone blend.

loss of water as explained by DSC explanation by Saxena *et al*. (24) and Qosim *et al*. (25) in DSC. The later endothermic peaks at 114.75 and 162.38 oC for erythromycin-povidone and erythromycin-β-cyclodextrin complexes respectively can be attributed to change of solid state to mesophase state of isotropic liquid. The lowest endothermic peaks for erythromycin-povidone and erythromycin-β-cyclodextrin complexes were observed at 87.50 and 87.45 °C respectively while the lowest endothermic peaks for unattached erythromycin, povidone and β-cyclodextrin excipients were observed at 92.40, 92.33 and 127.16 °C respectively. These low endothermic peaks are attributed to melting of undissolved material (24, 25). This shows that undissolved erythromycin-polymer complexes required lower melting temperatures compared to the temperatures required to melt its undissolved unattached components. The DSC thermogram curve of erythromycin–polymer complexes remain relatively unchanged from the combined effect of its constituents, and this can be attributed to simple hydrogen bonding from van der Waals interaction and non-chemical complex reaction as interpreted in compatibility behaviour by Fathy *et al*. (26). Erythromycin-polymer complex had reduced melting point and improved solubility without altering the chemical nature of erythromycin.

3.1.2. FT-IR spectrum

FT-IR determination results of powders and blends are presented in figure 2. The FTIR spectrum OH stretch vibration at 3261–3231/ cm for erythromycin was observed in the erythromycin-polymer blends. The functional aromatic carboxyl group stretch for erythromycin at 2952 / cm wavelength was observed in the erythromycin-polymer blends. The C=O stretch for erythromycin at 1743 - 1697 / cm wavelength was observed in the erythromycin-polymer blends. The CH and NH stretch for erythromycin at 592 - 607 / cm was observed in the erythromycin-polymer blends. These result indicates that the erythromycin functional groups were retained in the erythromycin-polymer blends. This suggests compatibility between the erythromycin and the β-cyclodextrin and povidone polymers, and aligns with other studies on compatibility and chemical stability by researchers such as Ali *et al*. (27).

3.1.3. SEM images

SEM images of powders and blends are presented in Figure 3. Pure erythromycin image showed well defined compact structures dissimilar to the image of starch. SEM images of β-Cyclodextrin showed irregular morphology while the SEM images of povidone were compact like starch but not spherical. The SEM images of β-Cyclodextrin-erythromycin and povidone-erythromycin complexes adopted irregular amorphous

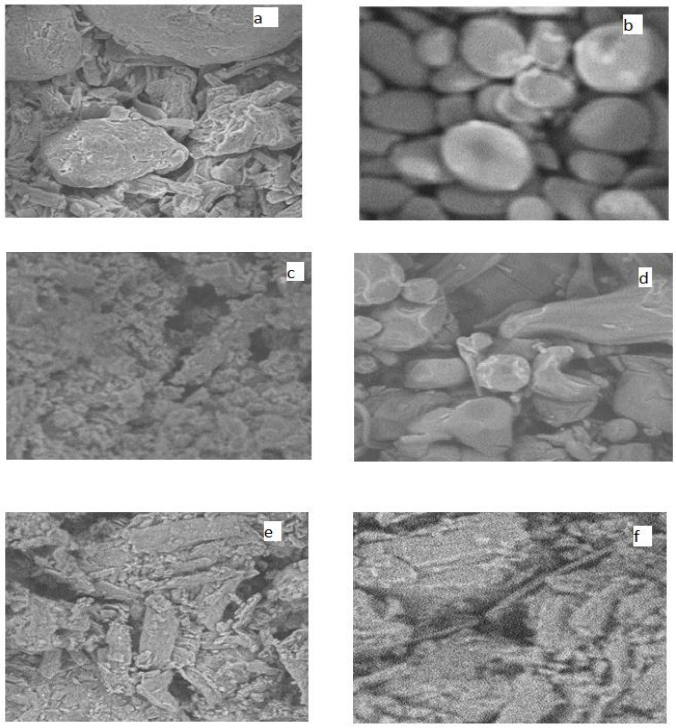

Figure 3. Scanning Electron Microscopy Images of Powders and Blends.
Key: a = erythromycin, b = starch, c = β-cyclodextrin, d = povidone, e = erythromycin – β-cyclodextrin blend, f = erythromycin – povidone blend.

polymer structures. These results are in consonance with previous reports such as Ali *et al*.(28) on material morphology.

3.2. Granules properties

3.2.1. Micromeritics properties

The micromeritics properties of the granules are presented in Table 2. They show granules Carr's index, Hausner ratio, and angle of repose ranges of 10.53-24.07 and 1.11-1.31, 21.43-30.51 ° respectively. These results indicate passable to good flow properties necessary for capsule filling with batches H>G>C>D>E>F>A>B. Batch H showed good to excellent flow properties which can be related to its higher concentration of starch used. This result agrees with the functional properties of starch as reported by researchers such as Wang and Ren (29) on the rheological, textural, pasting and flow properties of starch. Adding povidone to starch, Batch G, maintained the good flow properties of the granules. Batch A created heavier and faster falling flow rate (1.69 g / sec) granules that can be attributed to the higher binder and binding effect of the combined povidone and β-cyclodextrin polymers.

3.2.2. Drug loading and drug entrapment efficacy

The drug entrapment efficacy of the poly-

Table 2. Micromeritic Properties of Granules.

Batch	DEE (%)	Carr's Index (%)	Hausner ratio	Angle of repose (°)	Flow rate (g/sec)
A	99.26 ± 0.42	21.80 ± 0.16	1.28 ± 0.02	23.42 ± 0.42	1.69 ± 0.01
B	98.53 ± 0.41	24.07 ± 0.09	1.31 ± 0.01	21.60 ± 0.43	1.49 ± 0.01
C	99.73 ± 0.42	16.07 ± 0.09	1.19 ± 0.01	21.43 ± 0.42	1.36 ± 0.04
D	99.40 ± 0.19	19.37 ± 0.45	1.21 ± 0.02	24.41 ± 0.43	1.29 ± 0.01
E	98.93 ± 0.93	20.20 ± 0.16	1.25 ± 0.04	25.12 ± 0.09	1.34 ± 0.04
F	99.13 ± 0.44	20.53 ± 0.41	1.25 ± 0.04	30.37 ± 0.45	1.34 ± 0.04
G	98.67 ± 0.51	14.10 ± 0.14	1.15 ± 0.04	30.51 ± 0.41	1.44 ± 0.04
H	99.87 ± 0.91	10.53 ± 0.41	1.11 ± 0.01	22.53 ± 0.37	0.99 ± 0.09

Table 3. Physicochemical Properties of Capsules

Batch	Weight (mg)	D.T (min)
A	498.67 ± 1.25	13.33 ± 0.47
B	502.33 ± 0.47	24.67 ± 0.24
C	498.33 ± 0.47	15.53 ± 0.05
D	502.00 ± 0.00	12.53 ± 0.05
E	504.33 ± 0.94	10.73 ± 0.47
F	500.33 ± 0.47	06.33 ± 0.24
G	502.67 ± 0.47	12.67 ± 0.24
H	501.67 ± 0.94	14.87 ± 0.09

NB: DT = Disintegration time.

mers was > 97.81 %.

3.3. Capsule properties

3.3.1. Weight uniformity

The capsule weight variations are presented in Table 3. The capsules weight range of 498.33 – 504.33 mg is within the USP Pharmacopoeia weight uniformity specification of < 1 % deviation for 500 mg capsule.

3.3.2. Disintegration time

Disintegration time of capsules are presented in Table 3. Formulations with only povidone polymer or high amounts of bulking agent starch (batches G or H) or disintegrant avicel (batches A, D, E, and F) disintegrated in <15 min. This showed the disintegrant effect of povidone, avicel and starch. This result is in agreement with works by Hiremath et al. (6) on the improved functional properties of povidone when applied as a granulating agent.

3.3.3. Dissolution rate

Capsule dissolution rates are presented in Figure 4. The onset of dissolution in acidic pH was faster for Batch E>D>F>C>H>G>B>A. After 90 min in acidic pH, the rate of dissolution of E>D>C>G>H>F>B>A. At basic pH, the rate of dissolution of E>C>D>F>G>H>A>B. By 180 min, all the batches, except batch B, had dissolved about 100 % erythromycin. Formulation with povidone and avicel showed faster onset of dissolution than formulations without them. Avicel can be said to function by attracting water and disintegrating from capsule and granules. Povidone can be said to function by improving water affinity and agrees with the work of Grant *et al*. (5) on improvement of solubility of poorly water soluble drugs by povidone. These results indicate that povidone is a better drug entrapper for dissolution enhancement of erythromycin in comparison with β-cyclodextrin, and conforms to studies by Shoukat *et al*. (30) on enhancement of drug solubility.

3.3.4. Antimicrobial susceptibility

The susceptibilities of Staphylococcus sp to erythromycin capsules are presented as zones of inhibition in Table 4. Using the interpretation of Giuliano *et al*. (31), the organism, Staphylococcus sp. used in the studies showed susceptibilities to erythromycin. The pure (un-entrapped) erythromycin and other Batches H and F at peak 25 mg / ml concentration, with zone of inhibitions range

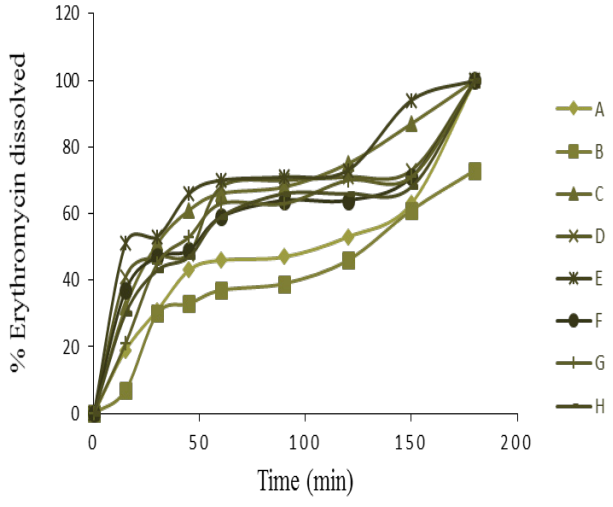

Figure 4. Dissolution Profiles of Erythromycin Capsules.

Table 4. Zone of Inhibition (mm) of Erythromycin Capsule Dilutions.

Batch	Concentrations of samples in water				
	25 µg / ml	12.50 µg / ml	6.25 µg / ml	3.13 µg / ml	1.57 µg / ml
CS	15.67 ± 0.47	6.67 ± 0.47	2.33 ± 0.47	2.00 ± 0.00	1.00 ± 0.00
A	33.67 ± 0.94	27.33 ± 1.25	17.00 ± 0.82	2.10 ± 0.00	1.00 ± 0.00
B	24.33 ± 0.47	22.91 ± 0.47	1.33 ± 0.47	1.00 ± 0.00	1.00 ± 0.00
C	29.33 ± 1.25	22.00 ± 2.16	16.33 ± 1.25	6.00 ± 3.56	2.00 ± 0.00
D	25.67 ± 0.94	21.33 ± 1.25	13.67 ± 0.47	2.67 ± 0.47	1.00 ± 0.00
E	39.83 ± 0.28	29.32 ± 0.56	18.00 ± 0.82	5.67 ± 0.94	1.00 ± 0.00
F	19.00 ± 0.82	6.00 ± 0.82	1.00 ± 0.00	1.00 ± 0.00	0.00 ± 0.00
G	37.67 ± 0.94	30.00 ± 0.82	15.00 ± 1.63	5.67 ± 0.47	1.33 ± 0.47
H	18.67 ± 0.94	10.00 ± 0.82	1.00 ± 0.00	1.00 ± 0.00	0.00 ± 0.00

NB: CS= Pure erythromycin active control sample.

of 14.00 – 22.00 mm, and is in line with erythromycin activity reported by other researchers such as Mutahhar and Puspitasari (32). At 25 mg/ml concentration, erythromycin-povidone entrapment with and without disintegrant (Batches E and G) gave the highest zone of inhibitions >39.83 and >37.67 mm respectively. At 25 mg/ml concentration, erythromycin- β-cyclodextrin entrapment with or without disintegrant (Batches B and D) gave better zone of inhibitions of >25.67 and >24.33 mm respectively, than the >15.67 zone of inhibition of un-entrapped erythromycin (CS). At same 25 mg/ ml concentration, Batches F and H with avicel disintegrant and starch diluents alone with pure erythromycin respectively, improved the 15.67 mm zone of inhibition of pure erythromycin to > 19.00 mm and 18.67 mm respectively. At concentrations 25.00 - 12.50 mg / ml, Batches A, B, D, E and G showed Staphylococcus susceptibility with zone of inhibition > 23 mm. The result showed that 25 mg/ml and 12.50 mg/ml Batch G (povidone-erythromycin complex) had the highest zone of inhibition, while pure erythromycin (CS) had the least zone of inhibition at similar concentrations 25 mg/ml and 12.50 mg/ml. The susceptibility of Staphylococcus followed this order G>E>A>C>D>B>F>H. Povidone and β-cyclodextrin improved antimicrobial activity of the Erythromycin and this could be attributed to the increased solubility and release rate from their complexes. This result conforms to reports of improvement in antimicrobial properties of modified erythromycin by researchers such as such as Platon *et al*. (12), Kempe *et al*. (13), Cyphert *et al*. (14) and Yu *et al*. (15). The antimicrobial result from this study is however limited by potential error from the source of Staphylococcus and type of β-cyclodextrin as explained by Platon *et al*. (12).

4. Conclusion

The erythromycin-povidone complex showed seemingly better erythromycin capsule dosage formulation, drug release properties and antimicrobial properties compared to erythromycin- β-cyclodextrin complex. This study is limited to the source of erythromycin and batch of β-cyclodextrin used. The findings may not be generalizable to the exact extent of these erythromycin - polymer complexes on erythromycin antimicrobial activity. There is need for further studies involving broader sources of β-cyclodextrin and erythromycin, and human clinical trials to ascertain and compare the stability, *in vivo* release, permeability and therapeutic properties of these erythromycin complexes.

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Conflict of Interest

The authors declare no conflict of interest.

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