Physicochemical and antimicrobial properties of microencapsulated seed extract of *Acacia nilotica* (Mimosaceae)

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ABSTRACT

Background: Microencapsulation is an easy and inexpensive means of delivering bioactive substances and has been employed in food industries, agriculture for fertilisers, and drug stability in pharmaceuticals.

Objective: The objective of this study was to design *Acacia nilotica* extract as microcapsules, evaluate its physicochemical and *in vitro* antimicrobial effect in selected microorganisms.

Methods: The absorption maxima and the Fourier-transform infrared spectrum of the extract were obtained. Microencapsulation was done by ionotropic gelation. The microcapsules were evaluated for particle size, swelling index, entrapment efficiency, drug release and antimicrobial activity. Data were analysed using analysis of variance and Dunnet's multiple comparison tests.

Results: The wavelength of maximum absorption for the extract was 208 nm and FTIR revealed functional groups indicating alkaloids, phenols and aromatic compounds. The particle sizes of the capsules increased with the increase in the amount of extract. Microcapsules having higher extract concentration showed lower swelling and higher entrapment efficiency. In addition, the release times (t_{50} and t_{80}) revealed controlled release, whilst the release kinetics followed Korsmeyer-Peppas model. The activity of the extract and its formulations appeared higher for the fungi compared to the bacteria.

Conclusion: *Acacia nilotica* extract was successfully formulated into microcapsules with acceptable physicochemical and antimicrobial properties

Key-words: *Acacia nilotica* extract; microcapsules; physicochemical properties; antimicrobial effects

Propriétés physicochimiques et antimicrobiennes de l'extrait de graines microencapsulées *d'Acacia nilotica* (Mimosaceae)

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RÉSUMÉ

Contexte: La micro-encapsulation est un moyen simple et peu coûteux d'administration des substances bioactives et a été utilisée dans les industries alimentaires, l'agriculture pour les engrais et la stabilité des médicaments dans les produits pharmaceutiques. L'objectif de cette étude était de concevoir l'extrait *d'Acacia nilotica* sous forme de microcapsules, d'évaluer son effet physicochimique et antimicrobien *in vitro* sur des micro-organismes sélectionnés.

Méthodes: Les maxima d'absorption et le spectre infrarouge par transformée de Fourier de l'extrait ont été obtenus. La micro-encapsulation a été réalisée par gélification ionotrope. Les microcapsules ont été évaluées pour la taille des particules, l'indice de gonflement, l'efficacité de piégeage, la libération du médicament et l'activité antimicrobienne. Les données ont été analysées à l'aide d'une analyse de variance et des tests de comparaison multiples de Dunnet.

Résultats: La longueur d'onde d'absorption maximale de l'extrait était de 208 nm et le l'IRTF a révélé des groupes fonctionnels indiquant des alcaloïdes, des phénols et des composés aromatiques. La taille des particules des capsules augmente avec l'augmentation de la quantité d'extrait. Les microcapsules ayant une concentration d'extrait plus élevée présentaient un gonflement plus faible et une efficacité de piégeage plus élevée. En outre plus, les temps de libération (t_{50} et t_{80}) ont révélé une libération contrôlée, tandis que la cinétique de libération suivait le modèle de Korsmeyer-Peppas. L'activité de l'extrait et de ses formulations semble plus élevée pour les champignons que pour les bactéries.

Conclusion: L'extrait *d'Acacia nilotica* a été formulé avec succès en microcapsules présentant des propriétés physicochimiques et antimicrobiennes acceptables.

Mots-clés: Extrait *d'Acacia nilotica* ; microcapsules ; propriétés physico-chimiques ; effets antimicrobiens

INTRODUCTION

For over three decades, the preference of herbal medicines over conventional drugs for the treatment of various ailments is continuously extending.[1] An estimate of 80% persons worldwide is known to depend on herbal medicines for the management or treatment of certain diseases.[2] A prominent use of herbal medicine is in the treatment of microbial infections and many herbs have been reported to possess activity against a wide range of microorganisms.[3,4,5] The antimicrobial activity of herbs has been attributed to their ability to overcome the challenge of resistance from microorganisms which is a major downside in the antibiotic therapy.[6] Herbs contain secondary metabolites such as alkaloids, flavonoids, polypeptides and flavones, which are responsible for their diverse biological and pharmacological activities.[4] Diverse modes of action of herbs have also been reported to reduce the occurrence of antimicrobial resistance.[5] The use of conventional medicine is also limited because of its toxicity, side effects and adverse drug reactions.[1] These limitations have promoted the use of herbal medicines based on the claims that they have lower propensity to induce toxicity or adverse effects.[7,8] The use of herbs for various ailments has been in existence for centuries and the presentation as being in different forms, such as decoctions and infusions. Some disadvantages of decoctions and infusions include lack of dosing accuracy, unpleasant taste and odour, which reduces patient acceptability.[9,10] To this effect, numerous efforts have been put in to develop, standardise and evaluate the efficacy of varying dosage forms containing herbal preparations.[11] To expand the scope of herbal drug delivery, the study employed microencapsulation technology for the delivery of *Acacia nilotica* fruit extract.

Previous studies.[12,13] have shown the use of polymers (synthetic, semi-synthetic or natural) to trap active ingredients within a membrane or shell to form microcapsules. The advantages of microcapsules include improved drug stability, controlled release properties, and enhanced taste for bitter drugs.[7] Microencapsulation is an easy method of preparing a bioactive agent as dosage form and has been used both in the food and agricultural industries for varying purposes.[14] Microencapsulation has been used in herbal drug delivery; for example, previous studies used varying polymers to encapsulate a mix of herbal extracts intended for stress management by the non-solvent addition method.[15,16] In addition, microcapsules of plant powders of Zingiber officinale and Garcinia kola having antioxidant properties were prepared by ultra-sonic spray drying.[16] Following analysis, the technique was found to preserve the antioxidant properties of the encapsulated plants. Furthermore, the aqueous extracts from Garcinia kola and Hunteria umbellata seeds have also been microencapsulated via the counterion coacervation method in a study aimed at assessing the in vitro drug release properties of the formulation. It was also discovered that the microcapsules exhibited controlled release of the plant materials.[17] The leaves, bark, root, flower, pods and gum from *Acacia nilotica* Lam (Mimosaceae) commonly known as gum arabic tree have long been used ethnomedicinally to treat intestinal pains, diarrhoea, cold, congestion, coughs, dysentery, fever, haemorrhages, leucorrhoea, sclerosis, and so on. Several pharmacological studies have also confirmed its anti-cancer, anti-tumour, anti-scorbutic, astringent, antioxidant, antiplasmodial and diuretic activities.[18] These activities have been attributed to the relatively high amounts of phytocompounds including alkaloids, flavonoids, saponins, tannins, and so on contained in the plant.[19] The antimicrobial activity of this plant against a wide range of pathogenic organisms has been proven in several studies.[20,21] Aremu *et al*.[22], recently reported that the antibacterial properties of *Acacia nilotica* extract showed significant activity against tested pathogens at 10 %w/w. There has not been any reported study on the oral formulation of *Acacia nilotica* extract as microcapsules and its physicochemical parameters against selected microorganisms; thus, necessitating the conduct of this study.

MATERIALS AND METHODS

The materials used in this study include the fruit pods of *Acacia nilotica* plant, obtained from the botanical garden of the Nigerian Institute of Pharmaceutical Research & Development (NIPRD). It was identified, assigned a voucher number NIPRD/H/7008 and kept in the Institute's herbarium. Methanol (96 %v /v, Cat number-1699618339) was obtained from Loba Chemie in India, and sodium alginate (GQ9501404) from Carl Roth GmbH & Co, Karlsruhe, Germany.

Plant preparation and extraction

The dried seeds were removed from the pods, pulverised and sieved using the 600 μm mesh size to obtain uniform particle sizes. The sieved material was packaged in an airtight container and stored until further use. The powdered plant material (500 g) was extracted by maceration in methanol with intermittent agitation for 72 h. The mixture was filtered using a muslin cloth and the filtrate was concentrated using a rotary evaporator. The

concentrate was dried to a constant weight on a water bath maintained at 50 ^{o}C. The dried extract was weighed and stored in an air tight bottle.

Determination of absorption maxima and calibration equation for *Acacia nilotica* seed extract

One gram (1g) of the extract was placed in a 100 mL flask, and 50 mL of phosphate buffer pH 6.8 was added. The flask was agitated in a temperature regulated shaker for 1 h. The mixture was then filtered using a Whatman filter paper. The absorption spectrum of the filtrate containing the extract was obtained using an ultra-violet (UV) spectrophotometer (Model Cintra 6, Type GBC UV-Visible, GBC, Scientific Equipment Ltd, Victoria, Australia) and the wavelength for maximum absorption was determined. To obtain the calibration curve, different concentrations of the extract were prepared between 0.01 mg/mL and 0.1 mg/ mL in phosphate buffer, pH of 6.8. The absorbance of each concentration was taken at 208 nm and plotted against the various concentrations to obtain the calibration equation.

Fourier-transform infrared spectroscopy (FTIR) for *Acacia nilotica* fruit extract

The FTIR (FTIR-spectrum BX 273, Perkin-Elmer, USA) analysis of the *Acacia nilotica* seed extract samples prepared in potassium bromide (KBr) discs were recorded. The scanning range was 350 cm-1 - 4400 cm-1. The Table-driven infrared application software (IRPal 2.0) was used to determine the class, structure and assignment of functional groups according to the wavelength of the observed peaks in the spectra.

Microencapsulation of *Acacia nilotica* seed extract

Microcapsules of *Acacia nilotica* seed extract was produced following the method hereby described. Briefly, a dispersion of the extract (400 - 800 mg) was mixed with 10 %w/v sodium alginate solution until a homogenous dispersion of the drug and polymer was obtained. The resulting mixture was added drop wise into a beaker containing 2 %w/v calcium chloride solution using a syringe. The gelled beads were allowed to cure for 30 min, recovered and air-dried in petri dishes. The dried microcapsules were then weighed and stored in air tight containers.

Determination of the physicochemical properties of the microcapsules

The size and morphology of the microcapsules were determined using optical microscopy (Olympus Model 312545, Japan). To determine the swelling index, 100 mg of microbeads were soaked in 20 mL phosphate buffer at pH 6.8 and the weight of the beads was determined after 3 h and 24 h.

The swelling index was calculated using equation 1 below:

Swelling index =

(Change in weight/Initial weight) × 100 [Eqn 1]

To determine the entrapment efficiency of the drug-loaded microcapsules, an amount of microcapsules equivalent to 50 mg of *Acacia nilotica* extract was weighed and crushed in a mortar with a pestle and suspended in 50 mL of a phosphate buffer at pH 6.8. The mixture was then filtered and the absorbance of the filtrate was determined using a UV spectrophotometer (Gransmore Green, Felsted Dunmow Essex CM6 3LB England) at 208 nm and then the amount of drugs present as microcapsules was calculated using equation 2 below:

E (%) = Actual drug content/Theoretical drug content × 100 [Eqn 2]

Drug release study

Dissolution of the microcapsules was determined using the USP XXI Paddle method rotated at 100 revolutions per minute.31 The dissolution media used was phosphate buffer, pH 6.8, was maintained at 37±0.5°C. Microcapsules equivalent to 200 mg *Acacia nilotica* extract were placed in the dissolution receptacle. Samples (10 mL) were withdrawn at different time intervals up to 360 min and replaced with equal amount of fresh medium. The sample was filtered and appropriately diluted to 1 in 10. The amount of extract released was determined using UV spectroscopy at 208 nm and then calculated using the calibration equation which was described earlier. The dissolution profiles of the different formulations were obtained.

Kinetic modelling of release profiles

The results obtained from the dissolution test were fitted into various kinetic for models. The different equations used in determining the kinetics and mechanism of drug release include zero order, first order, Higuchi, Hixson-Crowell, and Korsmeyer-Peppas. Values of correlation coefficients were used to identify the model of best fit.

Antimicrobial activity determination

The formulations were tested against selected strains of clinically active microbes using standard procedures. The results obtained were compared with those of conventional antimicrobial agent used as controls.

Data presentation and analysis

All experiments were performed in triplicate and the data presented as mean ± standard deviation (SD). Statistical analysis was performed using one-way Analysis of Variance (ANOVA) using GraphPad Prism® 5 (GraphPad Software Inc., San Diego, USA). Dunnett's Multiple Comparison Test was used to compare the individual differences between the physicochemical properties. At 95% confidence interval, $p < 0.05$ was considered significant. Additionally, the microcapsule formulations obtained were analysed using the similarity factor (f2) on DD Solver (Microsoft Excel add-in, Excel 2016).

RESULTS

Properties of the extract

The result of the spectrophotometric analysis showed that *Acacia nilotica* extract exhibited principal absorption maximal at 208 nm with an absorbance peak of 0.514. This is presented in Figure 1. The functional group band of the extract obtained from FTIR are shown in Table 1 with the respective structure and assignment. The FTIR of the extract (Figure 2) showed different peaks and functional groups of alkaloids, phenols, aromatic compounds, carboxylic acids and many other useful functional groups.

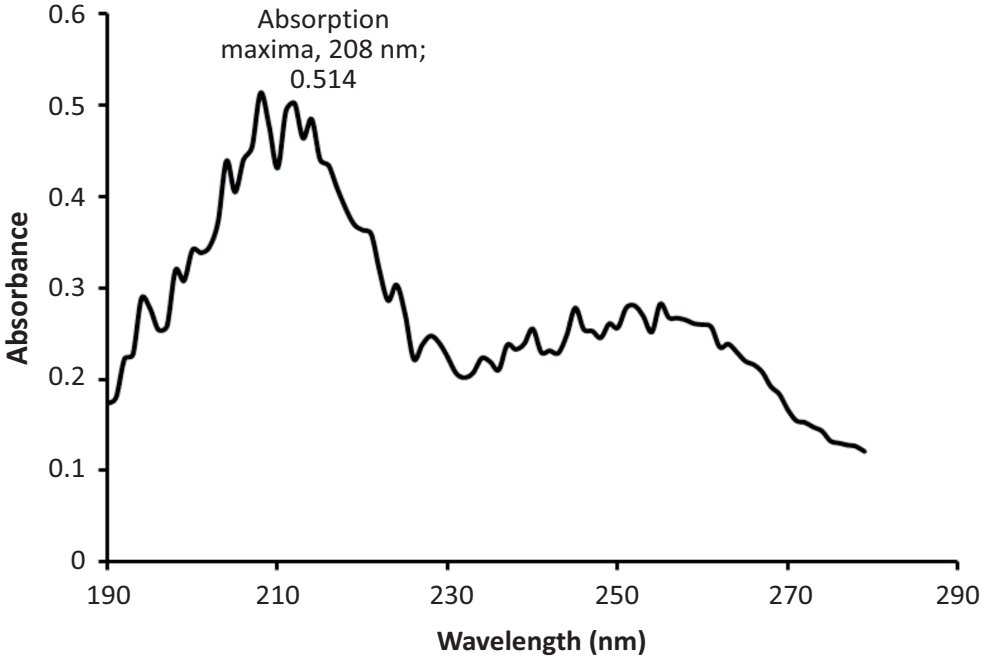

Figure 1: Graph of wavelength scanning for *Acacia nilotica* extract showing absorption

Table 1: Functional group bands of *Acacia nilotica* fruit extract obtained from FTIR spectra

Wavenumber (cm^{-1})	Class	Structure	Assignment
763.73	Aromatics	1,2,3 trisub	C-H out of plane
1112.35	Carboxylic acid	RCO-OH	C-O stretch
1282	Amines	Ar_2NH	Ar-N stretch
	Alkyl halides	R-F	C-F stretch
1390	Miscellaneous	S=O sulfate	S=O sulfate ester
1448.43	Miscellaneous	S=O sulfate	S=O sulfate ester
	Aromatics	C-C in ring	ArC-C stretch
1529.57	Miscellaneous	N=O Nitroso	N=O nitroso
1623	Amide	RCONH2	NH out of plane
	Amines	RNH2	NH2 in plane bend
2850-3000	Alkanes	RCH2CH3	CH stretch
3419	Alcohols	RCH2OH	O-H stretch
	Phenols	ArO-H bonded	ArO-H H-bonded
4355	Alkanes	RCH2CH3	CH stretch

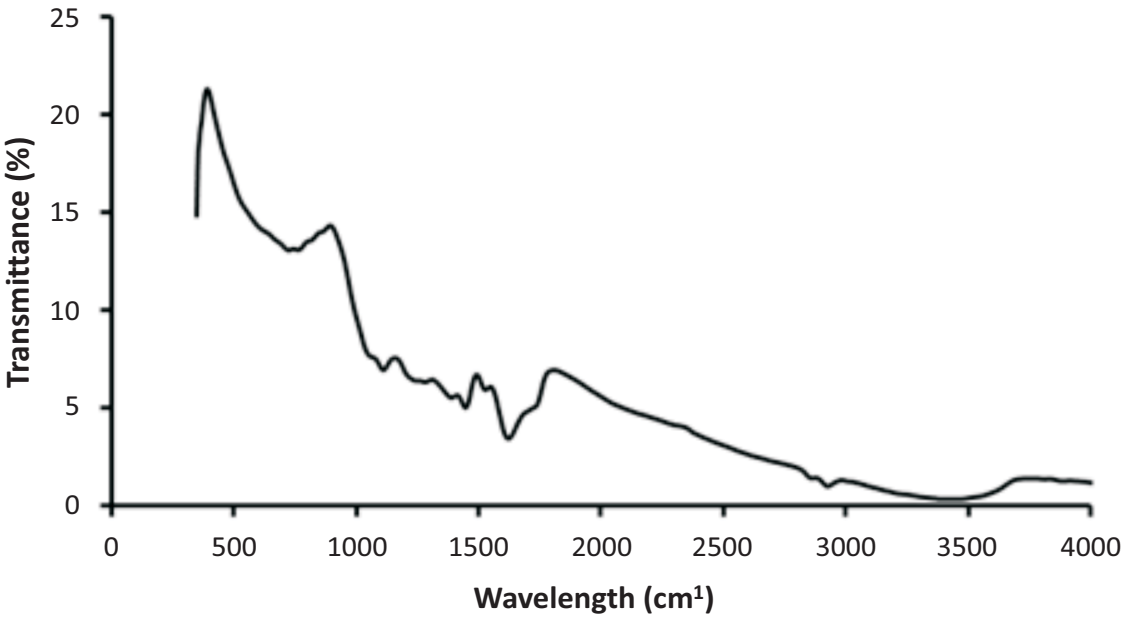

Figure 2: FTIR spectra for *Acacia nilotica* extract

Properties of the microcapsules

The particle sizes of the microcapsules are presented in Table 2. The sizes ranged from 1.63 mm ± 0.27 mm to 2.79 mm ± 0.44 mm. The results of the swelling index of the microcapsules are also presented in Table 2. The outcome showed that

Acacia nilotica microcapsules swelled with increasing time and the value at 24 h was significantly higher ($p < 0.05$) than at 3 h. In addition, the results of entrapment efficiency of the microcapsules are presented in Table 2. The entrapment efficiency of the formulations ranked AN800 > AN600 > AN400.

Table 2: The particle size, swelling index and entrapment efficiency of *Acacia nilotica* microcapsules

Code	Particle size (mm)	Swelling index (%)		Entrapment efficiency (%)
		3 h	24 h	
AN400	1.630 ± 0.267	55.4	80.4	41.23 ± 2.098
AN600	1.681 ± 0. 293	69.3	91.1	58.21 ± 1.307
AN800	2.792 ± 0.437	47.9	67.8	61.74 ± 2.024

The macroscopic appearance of the microcapsules in wet and dry forms during production is is shown in Figure 3. The microcapsules were discrete entities with spherical shapes during preparation and after drying. The photomicrographs are presented in Figure 4 and the spherical shapes are obvious for the microcapsules.

The release profiles of the microcapsules are presented in Figure 5. The figure showed that all the formulations demonstrated similar patterns at the early stage of release, as time increases, it became obvious that each formulation defined its own pattern. The results of dissolution times are presented in Table 3. The formulations showed similar t15 and t25; for t50 and t80, there was increase in the time taken for the drug to be released with increase in the amount of extract in the formulation.

The release kinetics of the formulations are presented in Table 4, with highest correlation coefficients ranging from 0.995 to 0.998 and followed Korsmeyer-Peppas model. Table 5 shows the results of the test of similarity for the release profiles amongst the microcapsules. The outcome showed that AN600 and AN800 were similar with f2 of 67.60, whilst the other formulations were dissimilar.

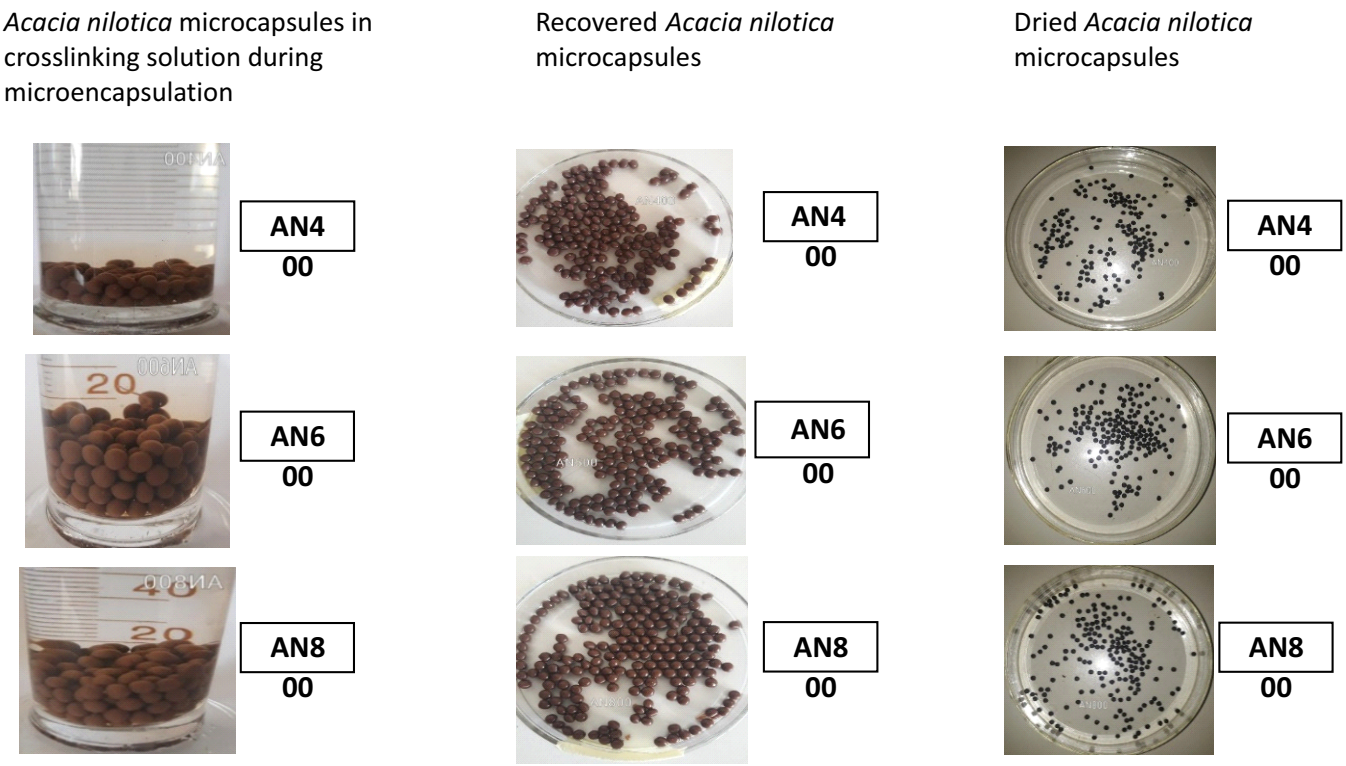

Figure 3: Macroscopic appearance of *Acacia nilotica* microcapsules during production

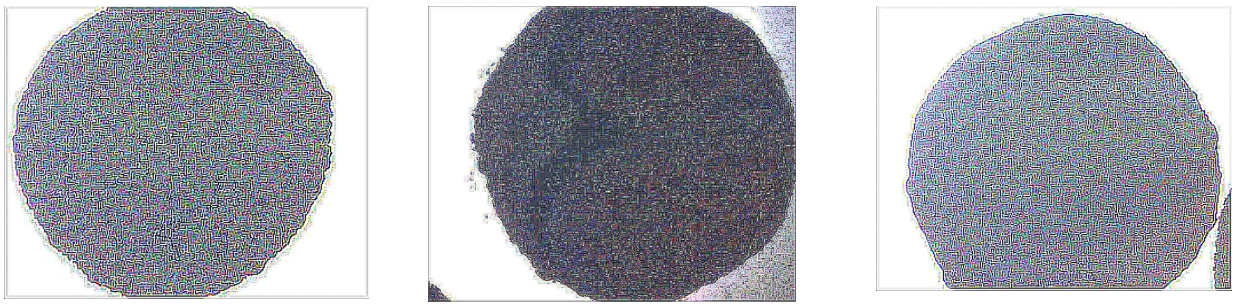

Figure 4: Photomicrographs of Acacia nilotica microcapsules (X40).

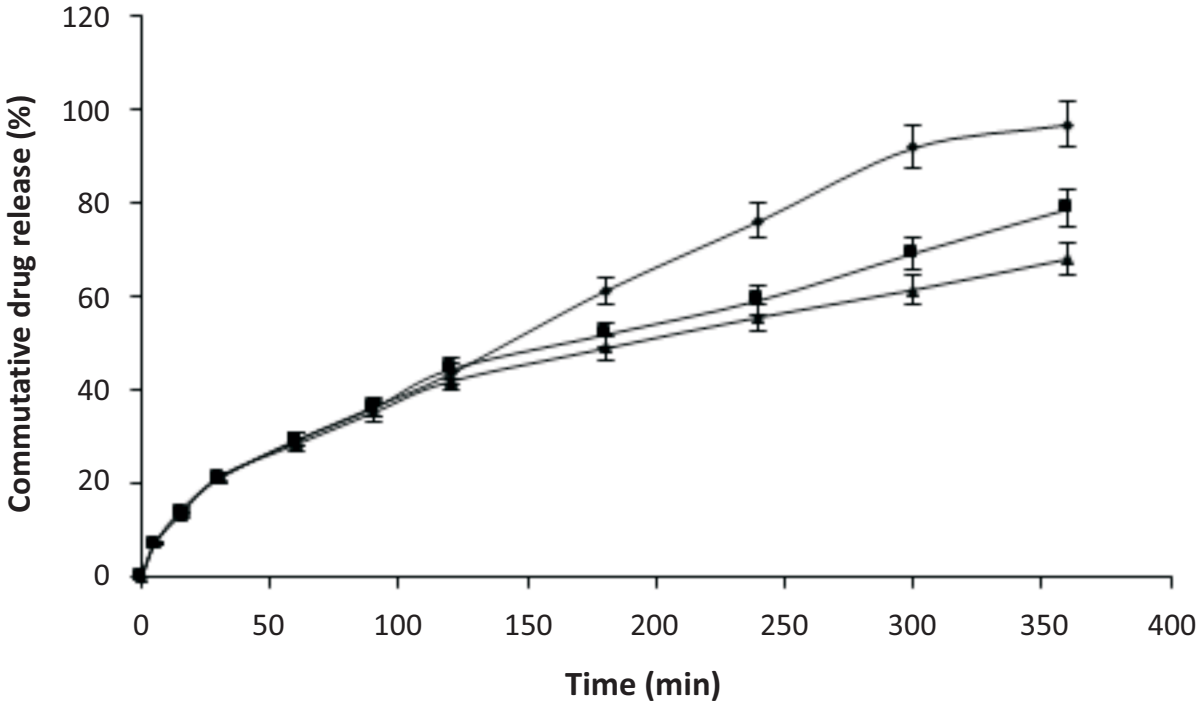

Figure 5: Release profiles of Acacia nilotica microcapsules (-AN400; <-AN600; 5-AN800)

Table 3: Dissolution times of Acacia nilotica microcapsules

Formulation code	t_{15} (min)	t_{25} (min)	t_{50} (min)	t_{80} (min)
AN400	20	47.32	131.44	202.80
AN600	21	45.35	162.90	387.67
AN800	20	45.59	190.62	502.88

Table 4: Release kinetics of Acacia nilotica microcapsules

Formulation code	Zero order	First order	Higuchi	Hixson-Crowell	Korsmeyer-Peppas	
	r^2					n
AN400	0.937	0.972	0.964	0.982	0.995*	0.678
AN600	0.835	0.960	0.995	0.935	0.998*	0.542
AN800	0.752	0.917	0.998	0.877	0.998*	0.485

**Highest correlation coefficients*

Table 5: The similarity factor (f2) obtained for comparing the release properties of Acacia nilotica microcapsules

Samples compared	Similarity factor (f_2)
AN400/600	48.84
AN400/800	41.79
AN600/800	67.60

The extract loaded with the microcapsules demonstrated antimicrobial activity on all organisms tested as shown in Table 6. The extract showed zones of inhibition ranging from 13.00 mm ± 1.41 mm to 15.50 mm ± 0.57 mm. The zones of inhibition for the extract-loaded microcapsules also ranged from 12.04 mm ± 1.22 mm to 16.45 mm ± 1.02 mm for the bacteria. The activity appeared higher for the fungi as it ranged from 15.00 mm ± 0.11 mm to 20.00 mm ± 2.83 mm.

Table 6: Zone of inhibition of *Acacia nilotica* microcapsules on the tested microorganisms

Formulation identification	*Klebsiella pneumoniae*	*Escherichia Coli*	*Staphylococcus aureus*	*Pseudomonas aeruginosa*	*Candida albicans*
	Zone of inhibition (mm)				
AN400	12.12 ± 0.27	15.23 ± 0.05	12.40 ± 0.14	–	15.00± 0.11
AN600	14.50 ± 0.32	16. 50 ± 0.33	15.25 ± 0.55	13.50± 0.23	17.00± 1.41
AN800	16.00 ± 0.05	16.45 ± 1.02	15.50 ± 0.95	14.00± 0.03	20.00± 2.83
Acacia nilotica extract	14.50 ± 0.11	13.00 ± 1.41	15.50 ± 0.57	12.05± 0.07	16.00± 1.41
Reference	20.00 ± 1.25	17.00 ± 2.83	26.00 ± 2.76	15.50± 1.54	35.50± 3.19
Sterile distilled water	–	–	–	–	–

DISCUSSION

The wavelength of maximum absorption was best taken when absorbance was nearly 1.0; however, if the peak wavelength is below 1.0, as it was in this case, then it has to be used. Non-linearity is generally caused by polychromatic light which is minimised whenever readings are taken at peak maximum. When absorbance measurements are above 1.0, there are problems of poor precision because of low intensity and curve linearity owing to stray light. Thus, the calibration curve was used to assess the properties of the microcapsules at a wavelength of 208 nm, and the linear regression equation for the plot of absorbance versus concentration was obtained as $y = 168.6x + 0.231$ with regression coefficient, $r^2 = 0.998$. In summary, the wavelength of maximum absorption (208 nm) taken for this extract was based on the factors discussed here to ensure optimal results.

Previous reports[23] in the literature have shown that Acacia nilotica contains alkaloids, volatile essential oils, phenols and phenolic glycosides resins, oleosins, steroids and tannins. Alkaloids are found in plants with at least one nitrogen atom attached to a carbon and hydrogen; the structure is basically that of amine.[24] Flavonoids have variable phenolic structures and generally contain functional hydroxyl groups through which they exhibit

their antioxidant properties.

The sizes of the microcapsules increased with increase in the amount of extract. Thus, AN800 had significantly higher ($p < 0.05$) particle size compared to the others. The particle sizes, however, indicated that the formulations contain microparticles and as more materials were added, the bulk was increased. Particle size is an important parameter in microcapsules as it influences the rate of dissolution which in turn affects absorption and the overall pharmacological effect of the dosage form. Swelling is crucial in microcapsules because it allows the entry of fluid into the particles. If there is no swelling, more fluid may not penetrate and the release of the active ingredient may be hampered. For AN800, swelling was significantly lower ($p < 0.05$) than for others. This could be attributed to the higher amount of extract which had occupied more spaces within the polymer thus limiting the interaction of polymer particles leading to a reduction in the swelling.

The entrapment thus increased with increase in the amount of extract loaded into the microcapsules. Generally, the entrapment of the microcapsules was satisfactory showing that the polymer used, that is sodium alginate was compatible with the extract for delivering appreciable drug loading. Previous study had reported in their study that sodium alginate could only load as much as 25% of drug needed for polymers enhancement.[25] Entrapment efficiency indicates the degree to which drug is implanted in the polymer system and it is a critical parameter for considering drug loading into microcapsules.

The release profile helps in assessing the success of a dosage formulation, especially when the controlled release rate of the drug is crucial. The figure for dissolution profiles showed that all the formulations demonstrated similar patterns at the early stage of release, as time increases, it became obvious that each formulation defined its own pattern. Definitely, the release was modified by the amount of extract loaded and the polymer. This is because as extract concentration was increased, the amount of polymer became reduced. Further analysis to determine the time taken for certain percentages (15, 25, 50 and 80%) of the drug to be released was also determined. The t_{50} and t_{80} showed that the formulations demonstrated controlled release of the drug. It indicates that the microcapsules acted fast at the initial period (less than 1 h) after ingesting it and the action will remain sustained as time progressed. Kinetic modelling is an important factor that provides evidence of the presence of drug and its concentration in the plasma. Applying the kinetic model is also strategic in clarifying mechanism of drug designing control.[26] Mathematical modelling is very useful in the study of drug release process. This is because it helps in designing the delivery system during a certain period, predicting the rate of drug release and avoiding undue experimental works.

The physical mechanism of drug release is determined by comparing the release data with mathematical models. This study can predict the effects of design parameters namely, shape, size and composition on the level of drug release as a whole and accurately envisage drug release profile to improve the overall therapeutic effectiveness and safety of the drug.[27] It is an important instrument for pharmaceutical drug preparations and determining in vitro and in vivo drug release processes. It resorts to model fitting on experimental release data and provides the measurement of some important physical parameters (e.g. drug diffusion coefficient).

The release kinetics of the microcapsules showed that it followed Korsmeyer-Peppas model, irrespective of the amount of extract within (Table 5). Korsmeyer-Peppas yielded the highest correlation coefficients (r^2 = 0.995-0.998). AN800 also yielded r^2 = 0.998 with Higuchi model. Korsmeyer-Peppas model of drug release is useful in describing the release from polymeric systems.[28] The rate of release of the model is related to the structural and geometric properties of the drug delivery systems, in this case the polymer (sodium alginate) serving as carrier. The model also provides a release exponent 'n' which corresponds to the mechanism of the release.[29]

Generally, in this study, the drug release from the microbeads was controlled by a combination of diffusion and erosion mechanisms. The release mechanism using the n value for most of the beads corresponds to mass transfer following a non-Fickian anomalous $0.5 < n < 1.0$ diffusion. Thus, the present result suggests that the more layers of encapsulation provide a denser matrix to give more protection for dissolution to the active metabolite.[30] The figures obtained in the release profile also support the goodness of Korsmeyer-Peppas model in describing an initial burst of release. For economic implications, AN600 will be preferred to AN800 to save the cost of producing more extract.

The microcapsules also showed antimicrobial activity dependent on extract concentration on all organisms

tested. It was observed that the formulation of microcapsules did not negatively impact on the zones of inhibition of the extract. However, there was a significant difference ($p<0.05$) between the zones of inhibition of *Acacia nilotica* microcapsules and the reference drugs both for the bacteria and fungi. The reference drugs (ciprofloxacin for bacteria and ketoconazole for fungi) showed significantly higher ($p < 0.05$) activity. The formulation of *Acacia nilotica* extract into microcapsules has offered a presentable dosage form for this active agent, thus creating room for improving dosage compliance and adherence. This would enhance therapy and improvement in patient's quality of life.

CONCLUSION

Acacia nilotica extract exhibited principal absorption maxima at 208 nm. Fourier-transform infrared spectroscopy showed important functional groups. The extract was successfully prepared as microcapsules. with sizes in micrometer range. Swelling and drug entrapment were influenced by time and extract concentration respectively. The release was controlled and modified by the amount of extract loaded and the polymer. The release kinetics of the microcapsules were comparable to that of Korsmeyer-Peppas model with non-Fickian anomalous diffusion mechanism Thus, the microcapsules can be further improved for translational outcomes in antimicrobial therapy.

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