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Solid-state Characterization and Evaluation of Native and Thiolated *Cedrela odorata* Gum in Ibuprofen Tablet Formulations

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ABSTRACT

Background: Modified natural polymers are considered as suitable options for sustained-release drug delivery systems, due to their enhanced functional properties.

Objectives: In this study, solid state characterization and functional properties of native and thiolated *Cedrela odorata* gum as components in ibuprofen tablet formulations were investigated.

Methods: The phytochemical components of purified *Cedrela odorata* gum (COG) were evaluated prior to modification with thioglycolic acid to yield ThCOG. Powdered COG and ThCOG were characterized using phytochemical tests, particle density, flow properties, morphology, swelling indices and FTIR spectra as evaluation criteria. Ibuprofen formulations containing varying concentrations (2.5 % - 10 %w/w) of the gums and other excipients were directly compressed into tablets, mechanically assessed using friability and crushing strength tests, while release properties were assessed using disintegration time and dissolution rate tests. Results were analyzed using descriptive statistics (n ± SD).

Results: COG and ThCOG contain alkaloids, cardenolides and saponins, but devoid of tannins and starch. COG and ThCOG were angular and irregular in shape respectively. ThCOG had a lower swelling index value (0.51±0.11%) compared to COG (1.63±0.03 %). Crushing strength was in the order: COG > ThCOG, while friability properties were in the reverse order. FTIR spectrum of ThCOG showed characteristic thiol peak (2558.7 cm^{-1}), carbonyl stretching (1708.8 cm^{-1}) and ester band (1279 cm^{-1}), confirming thiolation, while retaining the basic structure. Drug release was slower in tablets containing ThCOG.

Conclusion: Thiolated *Cedrela odorata* gum showed improved mechanical, compressional and sustained release properties than the native gum, and has good potential when incorporated in sustained release formulations.

Keywords: *Cedrela odorata* gum; Thiolation; Ibuprofen tablets; Sustained drug release.

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Caractérisation à l'état solide et évaluation de la gomme native et thiolée de *Cedrela odorata* dans les formulations de comprimés d'ibuprofène

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RÉSUMÉ

Contexte : Les polymères naturels modifiés sont considérés comme des options appropriées pour les systèmes d'administration de médicaments à libération prolongée, en raison de leurs propriétés fonctionnelles améliorées.

Objectifs : Dans cette étude, la caractérisation à l'état solide et les propriétés fonctionnelles de la gomme de *Cedrela odorata* native et thiolée, en tant que composants de formulations de comprimés de comprimés d'ibuprofène, ont été étudiées.

Méthodes : Les composants phytochimiques de la gomme purifiée de *Cedrela odorata* (COG) ont été évalués avant sa modification par l'acide thioglycolique pour obtenir la ThCOG. Les poudres de COG et de ThCOG ont été caractérisées par des tests phytochimiques, la densité des particules, les propriétés d'écoulement, la morphologie, les indices de gonflement et la spectroscopie FTIR comme critères d'évaluation. Des formulations d'ibuprofène contenant différentes concentrations (2,5 % à 10 % p/p) de ces gommes et d'autres excipients ont été comprimées directement en comprimés. Leurs propriétés mécaniques ont été évaluées par des tests de friabilité et de résistance à l'écrasement, tandis que leurs propriétés de libération ont été évaluées par des tests de temps de désintégration et de vitesse de dissolution. Les résultats ont été analysés à l'aide de statistiques descriptives (n ± écart-type).

Résultats : La COG *et la* ThCOG contiennent des alcaloïdes, des cardénolides et des saponines, mais sont dépourvues de tanins et d'amidon. La COG et la ThCOG présentaient respectivement une forme angulaire et irrégulière. La ThCOG présentait un indice de gonflement plus faible (0,51±0,11 %) par rapport à la COG (1,63±0,03 %). La résistance à l'écrasement suivait l'ordre : COG > ThCOG, tandis que les propriétés de friabilité suivaient l'ordre inverse. Le spectre FTIR de la ThCOG présentait un pic caractéristique de thiol (2 558,7 cm^{-1}), un étirement de carbonyle (1 708,8 cm^{-1}) et une bande ester cm^{-1}), confirmant la thiolation, tout en préservant la structure de base. La libération du principe actif était plus lente dans les comprimés contenant de la ThCOG.

Conclusion : La gomme thiolée de *Cedrela odorata* a montré des propriétés mécaniques, de compression et de libération prolongée améliorées par rapport à la gomme native, et présente un bon potentiel lorsqu'elle est incorporée dans des formulations à libération prolongée.

Mots-clés : gomme de *Cedrela odorata* ; thiolation ; comprimés d'ibuprofène ; libération prolongée du médicament.

INTRODUCTION

The significance of an effective drug delivery system is to enable the release of active pharmaceutical ingredients to the desired site of the body for drug release and absorption, thereby producing the desired therapeutic response. Conventional drug delivery systems are often associated with problems such as poor bioavailability due to hepatic first pass metabolism and fluctuations in plasma drug levels. Lack of an effective drug delivery system significantly compromises the expected therapeutic outcomes.[1] Sustained delivery systems have become very popular, because they avoid the shortcomings associated with conventional immediate release drug delivery systems such as complete enzymatic degradation, gastrointestinal toxicity of certain drugs and more importantly, patient compliance with the therapy regimen.[2,3] Some synthetic polymers such as polyacrylic acid, polymethacrylic acid and polyethylene oxide have been reported to contain sustained release abilities when used as mucoadhesive drug carriers.[4] However, natural polymers have gained considerable attention over synthetic excipients due to inherent compatibility, biodegradability and low toxicity. Moreover, natural polymers (such as gums) are ubiquitous in the environment and can be derived by propagation of their sources.[5] Natural gums can be modified through various chemical processes to enhance their properties for specific applications. The modification of gums is done via various methods such as changing functional groups of gum, cross-linking with ions, grafting with polymers, sulfation, phosphorylation and thiolation. Chemical modification of gums not only minimizes drawbacks of natural gums, but also enhances their functions for specific drug delivery purposes.[5]

Thiolation is a well-established method to enhance the properties of polymers.[6] Thiolation is a chemical modification process that involves the introduction of a thiol group (-SH) on a polymer backbone. Polymers that are thiolated tend to be more hydrophilic due to their high water solubility and easily form hydrogen bonds with mucin, leading to mucoprotective functions.[5,6] This occurs due to the spontaneous formation of intra- and inter-disulfide bonds with mucosal layers (cysteine rich areas).[7] Oral administration remains the most common and convenient route of drug delivery and is generally preferred in drug development due to its safety and suitability for processing substances in the gastrointestinal tract. Tablets are the most predominant and frequently used oral medication form, not only because of the convenience of administration for patients, but also because of their cost-effectiveness in the manufacturing process.[8]

Cedrela odorata (Family: *Meliaceae*) also known as spanish cedar, the most common species among the *Cedrela*, is widespread in seasonally dry tropical and subtropical forests. It is an important timber tree and has become naturalised in Africa and south-east Asia. Previous studies have documented the use of the unmodified gum as an excipient (binder, emulsifier and disintegrant) due to its favourable rheological properties[9] however, potentials of the thiolated form of the gum remain underexplored.

Ibuprofen is a non-steroidal anti-inflammatory drug (NSAID) used to manage various conditions such as pain, inflammation, and fever. Ibuprofen tablets are associated with certain limitations such as short duration of action, rapid drug release, gastrointestinal irritation and poor compressibility.[10] Hence, Ibuprofen requires formulation approaches that would extend residence time, sustain drug release and also provide mucoprotection from the direct irritating effects of the drug, thereby optimizing therapeutic outcomes. In this study, *Cedrela odorata* gum was modified by thiolation and the functional properties were evaluated in concentration graded ibuprofen formulations, in comparison with similar formulations containing the unmodified gum.

MATERIALS AND METHODS

Materials

The materials used were powdered ibuprofen BP, magnesium stearate BP, corn starch BP, and lactose monohydrate USP (obtained as gifts from Bond Chemical Limited, Aawe, Oyo State). Ethanol (95 %v/v), thioglycolic acid, talc and distilled water were obtained from the Research Laboratories of the Department of Pharmaceutics and Pharmaceutical Technology, and Centre for Drug Discovery, Development and Production, Faculty of Pharmaceutical Sciences, University of Ibadan, Ibadan, Nigeria. The gum was obtained from the exudates of the trunk *Cedrela odorata* (Family: *Meliaceae*) available as a tree crop in the Botanical Gardens of the University of Ibadan, Ibadan, Oyo state, Nigeria. All the other reagents used were of analytical grade.

Thiolation of native *Cedrela gum*

Exactly 10 gm of native *Cedrela odorata* gum was weighed and transferred into a beaker. Then 5 mL of thioglycolic acid was measured into a cylinder and diluted

with distilled water to the 20 mL mark. The mixture was transferred into the beaker containing the gum and stirred thoroughly until a paste was formed. The paste was spread thinly on a slab and oven dried at 40±0.5 ^{o}C for a period of 12 h to obtain the dry thiolated gum.[7] The dried powder obtained was sieved (sieve 250 mm pore size) and stored in an air-tight amber bottle.

Phytochemical Tests

Phytochemical tests were carried out on native and thiolated *Cedrela odorata* gum to determine the presence of tannins, cardenolides, anthraquinones, saponins, flavonoids and starch.[11]

Test for tannins: Exactly 0.5 gm of powdered native (or thiolated) Cedrela odorata gum was mixed with 20 mL of deionized water, heated for 10 minutes and sieved while still hot. The resulting sieved solution was cooled, and 1 mL of 5 % iron II chloride reagent was added to the filtrate. The presence of tannins will cause the formation of a bluish black colouration with green layer.[11]

Keller-Killiani test: Exactly 2 mL of glacial acetic acid (containing a drop of iron III chloride) was added to 0.5 gm of powdered native (or thiolated) *Cedrela odorata* gum in a beaker. Thereafter, 1 mL of concentrated tetraoxosulphate VI acid was added to form an under layer. Cardenolides, if present, will form a brown ring and a bluish-green layer.

Test for anthraquinones: 2 mL of 10 % hydrochloric acid was added to 0.5 gm powdered native (or thiolated) *Cedrela odorata* gum and heated for 10 min. The extract was sieved while still hot and portioned with 2.5 mL of trichloromethane with gentle agitation. The trichloromethane layer was emptied into a clean test tube and the same volume of ammonia hydroxide was gently added with agitation. A rose-pink layer on the test solution indicates the presence of anthraquinones.[11]

Saponification test: Exactly 3 mg of powdered native (or thiolated) *Cedrela odorata* gum was mixed with 60 mL of deionized water in a beaker and left to stand. The formation of froths is confirmatory for the presence of saponins.

Ammonia test for flavonoids: Five drops of a 25 %w/v suspension of the native (or thiolated) *Cedrela odorata* gum were applied onto a filter paper and exposed to ammonia vapor. The formation of distinct yellow spots will confirm the presence of flavonoids.[11]

Test for starch: A drop of 0.1 N iodine solution was added to 0.5 gm of native (or thiolated) *Cedrela odorata* gum. The formation of a blue-black colour will indicate the presence of starch.

Bulk and Tapped Densities

Twenty grams (20 gm) each of native and thiolated gum was separately weighed into a graded measuring cylinder (100 mL). The height at which the powder reached was measured from which the volume and the bulk density were determined. The bulk density was calculated as the ratio of the mass of sample to the volume of the sample in the cylinder. 100 taps maintained at a height of 1.4 cm from the base were then applied to the cylinder containing each sample, after which the height and volume were measured and used to calculate the tapped density as the ratio of the mass of the sample to the tapped volume. The determinations for the bulk and tapped densities were done in triplicates for each of the samples.

Hausner's Ratio and Carr's Index

The values obtained from the bulk and tapped densities were used in calculating the Hausner's ratio fand Carr's Index for the native and thiolated gum samples as indicated below:

$$\text{Hausner's Ratio} = \frac{\text{Bulk Density}}{\text{Tapped Density}} \quad \text{(i)}$$

$$\text{Carr's Index} = \frac{\text{Tapped Density - Bulk Density}}{\text{Tapped Density}} \quad \text{(ii)}$$

The determination was done in triplicate for each of the sample

Swelling Index

To determine the swelling index, 5 gm of the native (or thiolated) gum was transferred into a 100 mL cylinder (V1), 90 mL of distilled water was added and the slurry was shaken for 5 minutes and then made up to 100 mL. The suspension was allowed to stand for 24 h and the sedimentation volume (V2) was measured. The swelling index was determined in triplicates for each sample and calculated using the equation:

$$\text{Swelling Index} = \frac{V2}{V1} \quad \text{(iii)}$$

Fourier Transform Infrared Spectroscopy

The FTIR spectroscopy of the native and thiolated gums were obtained on an IR spectrophotometer using KBr disk (approximately 2 mg samples in 200 mg Kbr). The scanning was done in the range 400 - 4000cm^{-1}. Plot of percentage transmittance (% T) versus wave number (cm^{1}) were created on the computer monitor. The plots were printed out and analyzed for the characteristic functional group present in the sample.

pH determination

Exactly one (1) gm of the native gum (or thiolated gum) was weighed and placed in a 100 mL beaker and distilled water was added to the 100 mL mark. The dispersion was allowed to hydrate for 3 hours before the pH was determined using a digital pH meter (Model 720 A, Thermo Electron Corporation, MA, USA).

Compression of Ibuprofen Tablets

Ibuprofen tablets were directly compressed using the formula in Table 1. The tablet press consisted of a removable die assembly containing a flat-faced and circular upper and lower punches with a die of diameter 10.5 mm. The punches and die were lubricated with a 2.0 %w/v dispersion of magnesium stearate in acetone prior to each compression. The tablets were compressed at a compressional force of 1000 kg and a dwell time of 1 minute. After ejection, the compressed tablets were stored over silica gel for 24 h to allow elastic recovery and hardening of the tablets to occur. The tablets were then kept in air-tight, amber-coloured containers before the tablet properties were evaluated.

Table 1: Variables employed in the formulation of directly compressed Ibuprofen tablets.

S/N	Ingredients	Percentages of ingredients/batches				
		I	II	III	IV	V
1	Ibuprofen (200mg)	50.0%	50.0%	50.0%	50.0%	50.0%
2	COG or ThCOG	0.0%	2.5%	5.0%	7.5%	10.0%
3	Corn Starch	10%	10%	10%	10%	10%
4	Magnesium stearate	1%	1%	1%	1%	1%
5	Lactose	qs	qs	qs	qs	qs

COG (*Cedrela odorata* gum) ThCOG (Thiolated *Cedrela odorata* gum)

Evaluation of Tablet Properties

Thickness and weight uniformity tests

The weights of twenty randomly selected tablets were accurately determined to within ± 1 mg using a Mettler-Toledo precision analytical balance (Mettler-Toledo incorporated, Switzerland), while the diameter and thickness of the tablets were precisely measured to within ± 0.01 mm using a digital caliper micrometer (Starrett 795 series, Attol, Massachusetts, USA), at a temperature of 27 ± 0.5 ^{o}C.

Crushing strength and friability tests

The crushing strength test was determined (in triplicates) using a tablet hardness tester (MHT-100, Model P&M 01, Pharma Aliance Group, Indonesia). A tablet from each batch was placed between the anvil and the spindle of the tester and after zeroing, the force (N) was applied. Results of only tablets that split cleanly into two halves were recorded. The friability of the tablets was determined

using a friability test apparatus (DBK Instruments, Mumbai-6, Model 40FTA01, India). Tablets were weighed together on an electronic balance and then transferred into the drum of the friabilator set at a speed of 25rpm for four (4) minutes. After the rotation was completed, the tablets were re-weighed from which the percentage loss was calculated using the formula below:

$$\text{Friability (\%)} = \frac{\text{Initial weight - Final weight}}{\text{Initial weight}} \times 100 \qquad \text{(v)}$$

Disintegration test

The disintegration time for the tablets from each of the tablets were determined in distilled water at 37 ± 0.5º C using the DBK disintegration testing apparatus (Type 40TDA01, India). The time taken for each tablet to break up and pass through the mesh screen was recorded. The mean disintegration time and standard deviation were calculated for each batch.

Dissolution test

The dissolution rate of the tablets was determined in phosphate buffer (pH of 6.8) as the dissolution medium using the DBK dissolution test apparatus (Type 40DRT01, India). Each tablet was placed in the cylindrical basket, which was lowered into 1 L of the dissolution medium (immersed in the water bath maintained at a temperature of 37 ± 0.5º C) before the basket was set to rotate at 100 rpm. was started. Aliquots of 5 mL were withdrawn at 5, 10, 15, 30, 45,60, 120. 180. 240 and 300 minutes respectively from the dissolution medium into a volumetric flask. Equivalent volume of the phosphate buffer maintained at the same temperature was used to replace the volume withdrawn at each interval. Absorbance of each sample was recorded at a wavelength of 221 nm using a UV spectrophotometer (Sp6 - 450 UV/VIS spectrophotometer, Pye Unicam, Middlesex, England).

RESULTS

Phytochemical Properties

The results of the phytochemical tests confirmed the presence of alkaloids, cardenolides, flavonoids and saponins in native and thiolated *Cedrela odorata* gum. Tannins, anthraquinones, and starch were absent in both gum samples.

Physicochemical Properties

The physicochemical properties of the native and thiolated *Cedrela odorata* gums are presented in Table 2.

Fourier Transform Infrared (FTIR) Spectra and Photomicrographs.

The FTIR spectra and the photomicrographs of the native and thiolated *Cedrela odorata* gums are presented in Fig. 1 and Fig. 2 respectively.

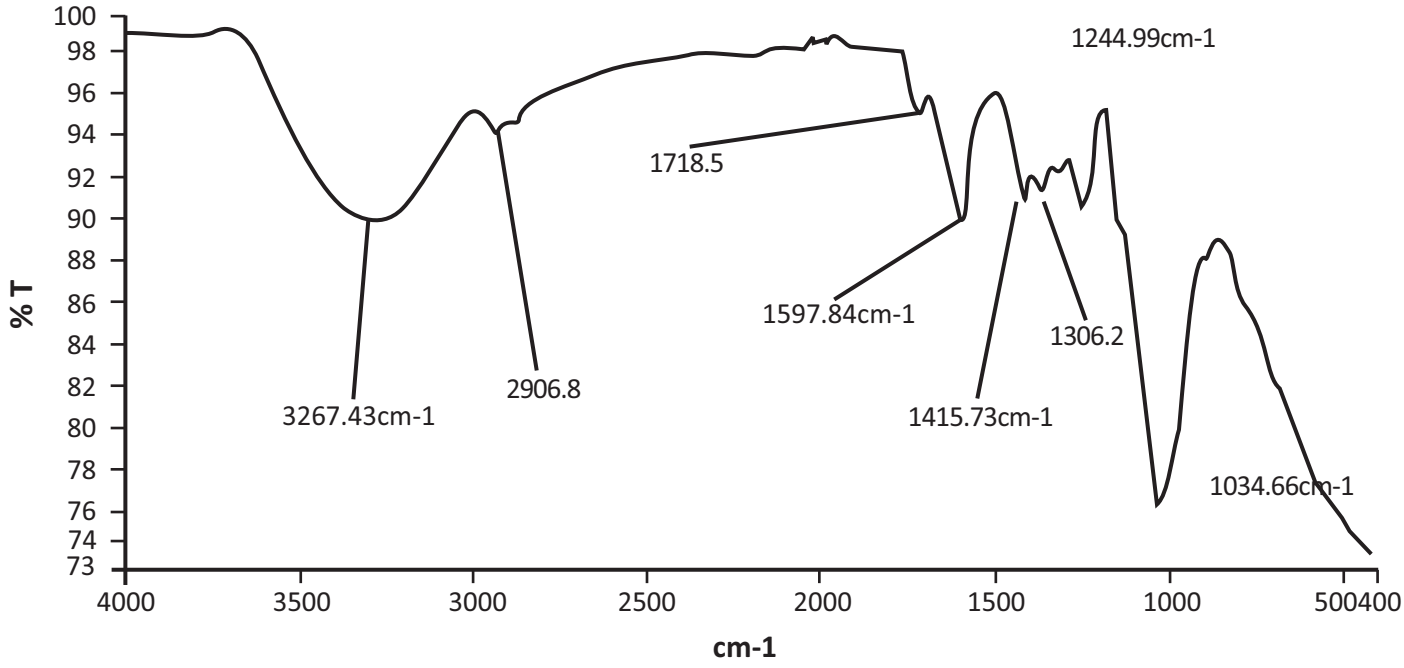
Physical, Mechanical and Release Properties of Tablets

The dimensions of the tablets are presented in Table 3, while the results obtained from the mechanical and release properties of ibuprofen tablets containing native and thiolated *Cedrela odorata* gum at different concentrations are presented in Table 4. The plots of the in-vitro release profiles of the ibuprofen tablets are presented in Fig. 3.

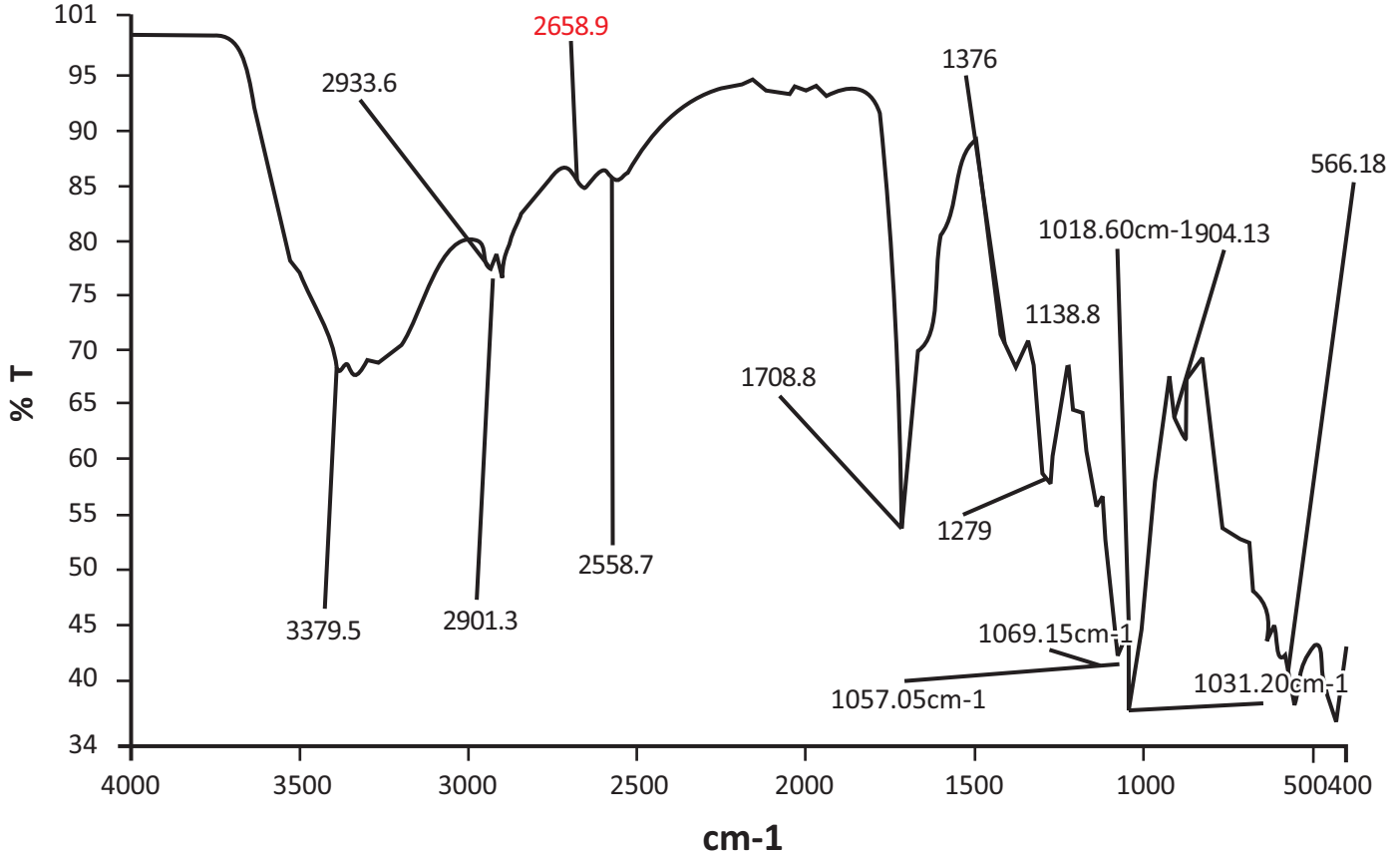
Table 2: Physicochemical properties (n=3 ± SD)

Parameters	Native *Cedrela odorata* gum	Thiolated *Cedrela odorata* gum
Particle shape	Angular	Irregular
Bulk density (g/cm^3)	0.833±0.012	0.667±0.005
Tapped density (g/cm^3)	0.909±0.002	0.714±0.013
Carr's index (%)	8.36±0.03%	6.58±0.04%
Hausner's ratio	1.09±0.01	1.03±0.01
Swelling index (%)	1.63±0.01%	0.5±0.01%
pH	5.75±0.13	4.71±0.04

Evaluation of collaborative care for patient medication management

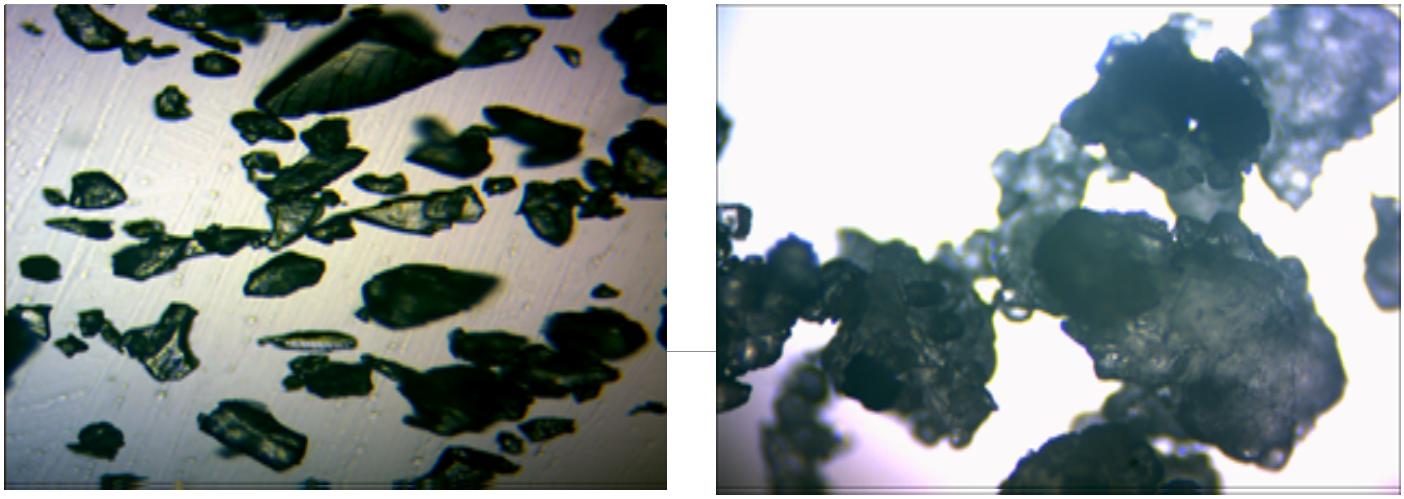


(a) Native *Cedrela odorata* gum



(b) Thiolated *Cedrela odorata* gum

Fig.1: FTIR spectrum of native and thiolated *Cedrela odorata* gum



(a)Native *Cedrela odorata* gum. X 400 (b) Thiolated *Cedrela odorata* gum. X 100

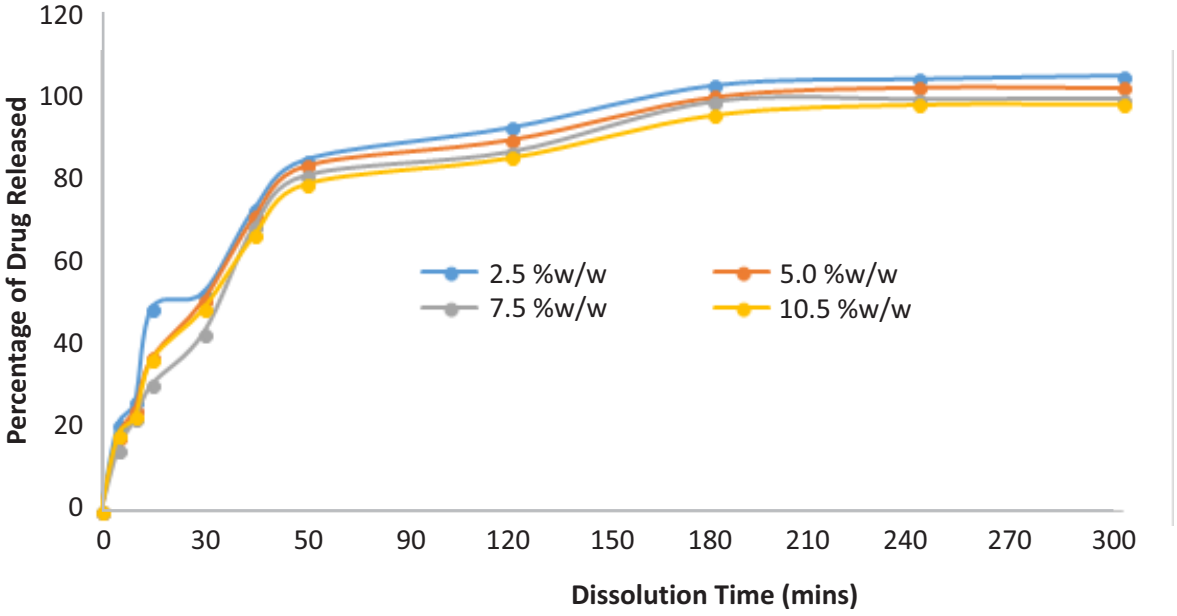
Fig. 2: Photomicrographs of native and thiolated *Cedrela odoranta* gum

Table 3: Physical properties (Dimensions) of ibuprofen tablets (n = 20 ± SD)

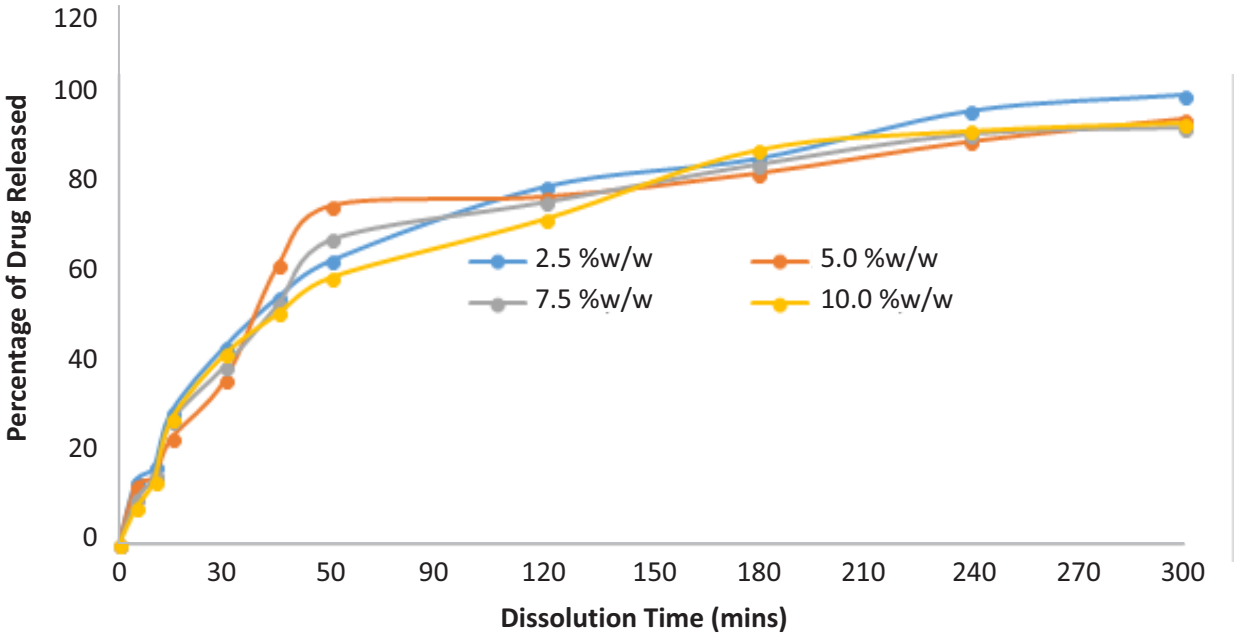
Type of Gum	Concentration of Gum (%w/w)	Tablet Thickness	Average weight of tablet (g)
	0.0	3.306 ± 0.130	0.361 ± 0.014
Native	2.5	3.323 ± 0.115	0.359 ± 0.012
Cedrela	5.0	3.276 ± 0.100	0.357 ± 0.008
odorata	7.5	3.309 ± 0.117	0.362 ± 0.009
	10.0	3.343 ± 0.119	0.362 ± 0.008
Thiolated	2.5	3.457 ± 0.086	0.372 ± 0.010
Cedrela	5.0	3.434 ± 0.102	0.380 ± 0,010
odorata	7.5	3.363 ± 0.116	0.379 ± 0.009
	10.0	3.304 ± 1.144	0.379 ± 0.008

Table 4: Mechanical and release properties of ibuprofen tablets

Type of Gum	Concentration of gum (%w/w)	Crushing Strength (N) (n=3 ±SD)	Friability (%)	Disintegration Time (min) (n=3±SD)	Dissolution Time (min) $t_{25\%}$	Dissolution Time (min) $t_{80\%}$
	2.5	15.46 ± 1.15	70.95	7.54 ± 0.03	9.25	52.02
Native	5.0	30.76 ± 1.92	53.51	9.18 ± 0.06	10.14	56.11
Cedrela	7.5	33.71 ± 0.31	53.14	11.88 ± 0.21	12.02	59.24
odorata	10.0	35.52 ± 0.18	44.25	11.21 ± 0.33	11.21	70.01
Thiolated	2.5	28.18 ± 1.31	1.71	9.75 ± 0.17	12.18	136.07
Cedrela	5.0	32.40 ± 1.98	0.89	11.86 ± 0.08	15.10	170.16
odorata	7.5	45.64 ± 0.25	0.99	12.36 ± 0.08	14.21	158.17
	10.0	48.14 ± 4.61	0.59	13.87 ± 0.14	14.25	154.13



a) Ibuprofen tablets containing native *Cedrela odorata* gum at different concentrations



(b) Ibuprofen tablets containing thiolated *Cedrela odorata* gum at different concentrations

Fig. 3: *In-vitro* dissolution profiles

DISCUSSION

Generally, the functional properties and polymeric behavior of polymers are inextricably linked to the bioactive compounds present in the plant.[12] Native and thiolated *Cedrela odorata* gum are devoid of tannins and anthraquinones, but contains alkaloids, cardenolides, saponins and flavonoids. Alkaloids are naturally occurring organic substances that have been documented to have antimicrobial, analgesic, and antimalarial effects on humans.[12] Cardenolides contain cardio-active steroids, while saponins contain triterpenoid steroids that have abilities to impair protein digestion, cause hypoglycemia and also possess antifungal activities.[13] Flavonoids play essential roles in many biological processes and responses to environmental factors in plant. They are common in human diets and have antioxidant effects as well as bioactivities, which reduce the risk of diseases.[14] The presence of the aforementioned constituents contributes to the overall functional activities of native

and thiolated *Cedrela odorata* gum, and care must be taken when incorporating them as excipients in formulations that contain active ingredients where the polymer may act as an adjunct.

Bulk density of powdered materials is crucial for packaging, transportation and storage, and is influenced by particle shape, size and size distribution, and the tendency of the particles to adhere to each other.[15] The thiolated *Cedrela odorata* gum showed a lower bulk density than the native gum. This may be due to the bigger size and irregularly shaped particles of the thiolated gum that had more void spaces, thereby hindering efficient packing resulting in lower bulk density.[15] Tapped density indicates the highest packing density of powder or blends of powders achieved under the influence of well-defined external forces. The highest packed volume achieved depends on a number of factors including particle size determination, true density, particle shape and cohesiveness due to surface forces including moisture.[16] The thiolated *Cedrela odorata* gum had lower tapped density compared to the native gum; this could be attributed to the finer particle size and angular morphology of the native gum. Several parameters such as Carr's index and Hausner's ratio can be used to assess the flow properties of materials.[17] Flow characteristics are improved when a material has a low compressibility index value, which can also be used to evaluate the potential of a material to reduce its volume when external pressures are applied.[18] The native and thiolated gum had Hausner's ratio and Carr's index less than 1.25 and 25 % respectively, indicating good flow properties.

Swelling index is a measure of the ability of a material to increase in volume at the absorbing surface by absorbing fluids available at the site of absorption; it is indicative of the extent of associative forces within the granules, therefore the higher the swelling index, the lower the associative forces, and the higher the tendency for drug release. This parameter is a primary requirement for initiation of sustained release models such as mucoadhesion.[19] The native *Cedrela odorata* gum had a higher swelling capacity than the thiolated gum. This could be attributed to the smaller size of the native gum, which had a higher tendency for moisture absorption than the larger sized thiolated gum. Moreover, hygroscopicity increases as the particle size of materials decreases.

The pH is a variable that can be used to determine the eligibility of a polymer for use in formulations that comes in contact with mucous membrane.[20] Values of pH for the gums are presented in Table 3.2 The pH of both the native (5.75 ± 0.13) and thiolated (4.71 ± 0.04) *Cedrela odorata* gum was within the 4.5 -7.0 specification of the United States Pharmacopoeia for dried gums.

Fourier Transform Infrared Spectroscopy (FTIR) is employed in identifying the functional groups present in compounds and can be used as an analytical technique for detecting drug-polymer interactions.[21] The functional group region of the FTIR spectra of the native gum shows a broad absorption band at 3267.43 cm^{-1}. This broad absorption band corresponds to O-H stretching vibration of hydroxyl groups involved in hydrogen bonding. The band at 2935.8 cm^{-1} is attributed to aliphatic methyl C-H stretching of the polysaccharide backbone. A sharp peak in 1778.5 cm^{-1} represents the C=O stretching of the carbonyl ion, likely arising from the esterified or uronic acid components.[21] The sharp peaks obtained at 1597.84 cm^{-1} and 1415.73 cm^{-1} show presence of asymmetric and symmetric stretching of carboxylate groups respectively. The absorption bands at 1338.2 cm^{-1} and 1244.98 cm^{-1} are associated with C-O stretching and O-H bending vibrations of polysaccharide rings. The prominent peak at 1034.60 cm^{-1} confirms C-O-C stretching of glycosidic linkages. The FTIR spectrum of the thiolated *cedrela odorata* gum shows a characteristic thiol peak at 2558.7 cm^{-1} along with a carbonyl stretching in 1708.8 cm^{-1} and ester-related band at 1279 cm^{-1}, confirming thiolation of the gum, while retaining the strong C-O-C stretching bands between 1057- 1018 cm^{-1}.

Generally, the shape of particles influences their arrangement at the initial stages of the compaction process. Several operation processes such as hopper feeding, discharge from hoppers, dosing and pneumatic conveying are also affected by the shape of particles.[22] The photomicrographs of the gums (Fig. 1) show that native *Cedrela odorata* gum is angular in shape, while the thiolated gum is irregularly shaped. Irregularly shaped particles tend to interlock and cause a reduction in flow, though impacting strength to the bed of particles. It is expected that the unmodified *Cedrela odorata* gum will exhibit better flow than the thiolated gum.[22]

The British Pharmacopeia states that for tablets with weight of 250 mg or more, a limit of ± 5 % deviation from the mean of the twenty tablets used is allowed.[23] The percentage deviation for the native formulations ranged from 0.04 - 9.32 % and for the thiolated formulations

ranged from 0.09 - 5.19 %. The tablet formulations that contained thiolated *Cedrela odorata* gum exhibited superior weight uniformity, indicating that thiolation improves binding efficiency, powder flow and compressibility, resulting in better weight uniformity compared to the tablet formulations that contained the native gum.

Hardness also known as crushing strength is a measure of the mechanical strength of tablet. It is defined as the force required to break a tablet diametrically under pressure. Adequate hardness ensures that the tablet does not break during handling and packaging. However, excessive hardness may impair disintegration and drug release. Crushing strength is the characteristic of a tablet that reveals its ability to resist permanent deformation.[24] The crushing strength values of the tablets were directly related to the concentration, however, tablets containing the thiolated gum had higher crushing strength values. Friability tests are employed to determine the physical strength of compressed and uncoated tablets on exposure to mechanical shock. The acceptable percentage loss in weight for compressed tablets is less than or equal to 1%.[24] The friability results indicated that thiolation enhanced the quality of the tablets based on these criteria as all the tablets containing the modified gum passed the friability test at high concentrations. Tablets containing the native gum were observed to be highly friable at all concentrations.

The release properties of the tablets were evaluated using disintegration and dissolution tests. Tablet disintegration is an important factor for drug release and could be the rate determining step in the process of the drug absorption.[25] A drug molecule must be present in solution before it can be absorbed and this requires an initial disintegration process.[25] The official requirement is that uncoated tablets for immediate release of the drug should disintegrate within 15 minutes.[25] Tablets formulated with native and thiolated Cedrela odorata gum passed the disintegration time test. The *in-vitro* dissolution plots for the formulations are shown in Fig. 3, while the time taken for 25 % ($t_{25\%}$) and 80 % ($t_{80\%}$) of the drug to be released are presented in Table 4. A good understanding of the kinetic pattern of drug dissolution helps the formulation scientist to design solid dosage forms that will meet the expected goal. Sustained release formulations are generally designed to prevent immediate release of the products and have been exploited for use in several oral formulations.[23] The tablets all showed a slow release at the commencement of the dissolution test. *Cedrela odorata* gum is a natural, highly hydrophilic polysaccharide that acts as a strong release retarding agent.[9] Across all concentrations, the dissolution test results showed that the time it took 80 % of the drug to be released for formulations containing 2.5 %w/w of native and thiolated gum (52.02 minutes and 136.07 minutes respectively) does not favour incorporating the gum as an excipient for immediate release formulations. The drug release pattern of the formulation indicated that the sulfhydryl (-SH) group attached to the backbone of the native gum in the thiolation process enhanced the sustained release of the formulations across all concentrations. This was probably achieved by improved cohesion and reduced erosion of the thiolated tablets.[26,27]

CONCLUSION

Thiolation of the *Cedrela odorata* gum improved the physicochemical properties of the native gum as evidenced by increased particle size and density, lowered Hausner's ratio and Carr's index which are indicative of an improvement in the flow properties of the native gum. The results of the release rates also suggest that thiolated *Cedrela odorata* gum will be more useful as an excipient in sustained than immediate release formulations as indicated from the initial release bursts which are indications of sustained activities of the formulations containing the thiolated *Cedrela odorata* gum.

REFERENCES

1. Nammas M (2025). The Impact of Drug Delivery Systems on Pharmacokinetics and Drug-Drug Interactions in Neuropsychiatric Treatment. *Cureus* 8 (17):1-6.
2. Ezike TC, Okpala US, Onoja UL, Nwike CP, Ezeako EC, Okpara OJ, Okoroafor CC, Eze SC, Kalu OL, Odoh EC, Nwadike UG, Ogbodo JO, Umeh BU, Ossai EC, Nwanguma BC (2023). Advances in drug delivery systems, challenges and future directions. *Heliyon* 24 (9): 6-12.
3. Shaikh R, Singh TRR, Garland MJ, Woolfson AD. Donnelly RF (2011). Mucoadhesive drug delivery systems. *Journal of Pharmacy and Biological Sciences* 3(1): 89 - 100.
4. Lele BS, Hoffman AS (2000). Mucoadhesive drug carriers based on complexes of poly(acrylic acid) and PEGylated drugs having hydrolysable PEG-anhydride-drug linkages. *Journal of Controlled Release* 69 (2): 237-248.
5. Jain S, Jain A, Jain R, Chauhan NS (2024). Potential of natural polymeric materials in pharmaceutics. *Pharmacological Research - Natural Products* 2: 1-14.
6. Puri V, Sharma A, Kumar P, Singh I (2020). Thiolation of biopolymers for developing drug delivery systems with enhanced mechanical and mucoadhesive

properties: a review. *Polymers* 12(8): 18-30.
7. Rana V, Kamboj S, Sharma R, Singh K (2015). Modification of gums: synthesis techniques and pharmaceutical benefits. In: VK Thakur, MK Thakur, eds: Handbook of Polymers for Pharmaceutical Technologies: *Scrivener Publishing*. Pp. 229 - 364.
8. Dudhat KR (2020). The overview of oral solid dosage and different excipients used for solid dosage form formulations. *Global Academic Journal of Pharmacy and Drug Research* 4(3): 66 -72.
9. Ayorinde JO, Odeniyi MA (2018). Solid state characterization of two novel gums from Cedrela odorata and Enterlobium cyclocarpum. *Journal of Pharmaceutical Investigation* 48(4): 487-496.
10. Smrčka D, Ramesh S, Dumicic A, Beránek J (2026): Optimizing ibuprofen dosing: insights from in vivo and virtual pharmacokinetic trials. *European Journal of Pharmaceutical Sciences* 220: 928-987.
11. Tiranakwit T, Puangpun W, Tamprasit K, Wichai N, Siriamornpun S, Srisongkram T, Weerapreeyakul N (2023). Phytochemical Screening on Phenolic, Flavonoid Contents, and Antioxidant Activities of Six Indigenous Plants Used in Traditional Thai Medicine. *International Journal of Molecular Science* 24(17):13-23.
12. Gupta S, Trupesh R, Himanshu P, Hitesh S (2025). Comparative analysis of the phytochemical profiles of selected edible gums. *International Journal of Molecular Science* 2(4): 217-224.
13. Wakte P, Bhusari SS, Pradhan S, Shinganapure SS (2025). Comparative analysis of natural versus synthetic polymers in mucoadhesive buccal drug delivery systems: A focus on xyloglucan-based platforms. *International Journal of Modern Pharmaceutical Research* 11: 33-39.
14. Shen N, Wang T, Gan Q, Liu S, Wang L, Jin B (2022). Plant flavonoids: Classification, distribution, biosynthesis, and antioxidant activity. *Food Chemistry* 18:323-353.
15. Rüther M, Klippstein SH, Ponusamy SK, Rüther T, Schmid H (2023). Flowability of polymer powders at elevated temperatures for additive manufacturing, *Powder Technology* 422: 2023-2037.
16. Bondi G, D'Abbrunzo I, Hasa D, Parolin C, Vitali B, Bertoni S, Imbriano A, Pagano C, Fratini C, Sabbatini B. Bigucci F, Abruzzo A (2025). Innovative bilayered buccal films: A paediatric-friendly dosage form for transmucosal azithromycin delivery. *International Journal of Pharmacy* 684:126-164.
17. Suhag R, Kellil A, Razem M (2024). Factors influencing food powder flowability. *Powders* 3(1): 65-76.
18. Ghasemi MZ, Hellstrom JGI, Umeki K (2025). Effect of particle irregularity and particle size distribution on the morphology of packed beds of biochar particles. *Scientific Reports* 201 (2):101-128.
19. Adetunji OA, Ajakore, OM, Itiola OA (2021). Physicochemical and Morphological Properties of Thermally Modulated Carboxymethylated Entandophragma angolense Gum. *European Journal of Pharmaceutical and Medical Research* 8: 96-103.
20. Maslii Y, Ruban O, Kasparaviciene G, Kalveniene Z, Materiienko A, Ivanauskas L, Mazurkeviciute A, Kopustinskiene DM, Bernatoniene J. (2020). The Influence of pH Values on the Rheological, Textural and Release Properties of Carbomer Polacril® 40P-Based Dental Gel Formulation with Plant-Derived and Synthetic Active Components. *Molecules* 25(21):50-68.
21. Gong Y, Chen X, Wu W (2024). Application of fourier transform infrared (FTIR) spectroscopy in sample preparation: Material characterization and mechanism investigation. *Advances in Sample Preparation* 11:100-122.
22. Monfared ZG, Hellström JGI, Umeki K. (2025). Effect of particle irregularity and particle size distribution on the morphology of packed beds of biochar particles. *Scientific Report* 29:15-20.
23. British Pharmacopoeia Vol. 1 and 2. British Pharmaceutical Press, Her Majesty's Stationary Office, London, 2010.
24. Singh Roy P, Biswas A, Pratihar S, Ghosh, AK (2025). Effect of binders on tablet hardness and disintegration time. International *Journal of Pharmaceutical Research and Applications* 10: 1612-1620.
25. Kayode AD, Adetunji OA (2024). Compression and release properties of two-step modified rice starch and lactose blends in paracetamol tablet formulations. *African Journal of Biomedical Research* 27: 343-348.
26. Puri V, Sharma A, Kumar P, Singh I, Huanbutta K (2021). Synthesis and Characterization of Thiolated Gum Ghatti as a Novel Excipient: Development of Compression-Coated Mucoadhesive Tablets of Domperidone. *ACS Omega* 10(24):15844-15854.
27. Kumar NR, Koteswara R, Vijaya Ratna J, Ramana-Murthy, KV (2024). Exploring the potential of neem and tamarind gum as release retardants: Design and statistical optimization of vildagliptin extended-release matrix systems using D-optimal quadratic mixture design. *International Journal of Biological Macromolecules* 259: 129-136.