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Formulation and Evaluation of Pharmaceutical Suspensions Using Hemicellulose Extracted from Oil Palm Empty Fruit Bunches

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Abstract

Oil palm empty fruit bunches (OPEFB), a major solid waste from palm oil processing, represent a rich source of lignocellulosic biomass that can be valorized into high-value bioproducts. This study aimed to isolate hemicellulose from OPEFB and evaluate its potential as a natural suspending agent in pharmaceutical suspension formulations, either alone or in combination with sodium carboxymethyl cellulose (CMC-Na). A series of formulations (F0–F5) were prepared and characterized for organoleptic properties, pH, density, viscosity, sedimentation volume, and redispersibility over seven days of storage. The results showed that suspensions containing OPEFB hemicellulose exhibited acceptable sensory characteristics, stable pH values (5–7), and densities above 1.00 g/mL. The addition of hemicellulose and CMC-Na significantly increased viscosity (up to 683.5 cP) and improved sedimentation stability, with sedimentation volumes reaching 0.22 and redispersibility up to 90% in formulations F2 and F3. These findings indicate a synergistic effect between hemicellulose and CMC-Na, enhancing suspension uniformity and preventing particle aggregation without compromising flowability. In conclusion, OPEFB-derived hemicellulose demonstrates excellent potential as a biodegradable and eco-friendly suspending agent for pharmaceutical suspensions. Its use not only improves formulation stability but also promotes the sustainable utilization of palm oil industry waste in green pharmaceutical product development.

Introduction

One of the primary waste products from palm oil processing is oil palm empty fruit bunches (OPEFB) derived from *Elaeis guineensis* Jacq. With the global increase in palm oil production, OPEFB constitutes the largest solid waste, accounting for approximately 20-23% of processed fresh fruit bunches, and poses environmental challenges if not properly managed, such as pollution from open dumping or burning (1,2). The utilization of OPEFB as a lignocellulosic biomass source has gained attention in recent research to support a sustainable bioeconomy, including its conversion into organic fertilizers, bioenergy, or high-value chemical products (3).

OPEFB is rich in lignocellulosic components, comprising cellulose (23.7-65%), hemicellulose (17.1-33.5%), and lignin (13.2-29.2%) on a dry weight basis, with variations depending on pretreatment and analytical methods (4,5). This composition makes OPEFB a promising raw material for polysaccharide extraction, although its high lignin content necessitates delignification to enhance the accessibility of cellulose and hemicellulose (6).

Hemicellulose, a heterogeneous polysaccharide, can be isolated from OPEFB through alkaline extraction methods, such as using NaOH or combined peroxide treatments, which effectively dissolve lignin and hemicellulose while preserving cellulose structure (7). A two-stage method, such as peracetic acid

pretreatment followed by alkaline peroxide, has been shown to yield up to 18.4% hemicellulose from dry OPEFB weight, optimized through Taguchi experimental design (8). Sequential oxidative approaches have also reduced residual hemicellulose to 5.2% after two cycles, producing high-purity hemicellulose for advanced applications (9). Hemicellulose from natural sources like OPEFB can be converted into products such as xylose or xylo-oligosaccharides, supporting industrial applications (10).

In the pharmaceutical field, hemicellulose exhibits multifunctional potential as a natural excipient, serving as a tablet binder, controlled-release agent, film coating material, and suspending or thickening agent due to its biocompatibility, biodegradability, and tunable viscosity (11,12). Hemicellulose from plant sources has been evaluated as a hydrogel, thickener, and stabilizer in drug formulations, capable of forming stable colloidal suspensions and enhancing drug bioavailability (13). Furthermore, hemicellulose derivatives like arabinoxylan have been utilized in hemicellulose-based films for controlled drug delivery, demonstrating non-Fickian release and antibacterial activity (14). Given these potentials, innovating the use of OPEFB-derived hemicellulose as a suspending agent in pharmaceutical suspensions is highly relevant, particularly as a sustainable and safer alternative to synthetic excipients (15).

Suspending agents are substances that increase solution viscosity, slow particle sedimentation, and ensure uniform distribution in suspensions, thereby supporting stability and accurate dosing (16). Suspensions are heterogeneous pharmaceutical preparations where insoluble solid particles are dispersed in a liquid phase, commonly used for drugs with low solubility or to improve palatability and bioavailability in pediatric patients (17). Natural suspending agents, such as mucilage from Aloe or plant-derived polysaccharides, have shown effectiveness in maintaining sedimentation volumes up to 94% and pseudoplastic viscosity, with applications in paracetamol suspensions (18). In developing pediatric suspensions, the selection of suspending agents must consider pH stability, particle size, and minimal excipient use to reduce toxicity risks (19).

Based on the above description, this study aims to develop a suspension formulation using hemicellulose from oil palm empty fruit bunches (OPEFB), contributing to the sustainable utilization of palm oil waste in the pharmaceutical industry.

Method

Materials

The equipment used in this study included laboratory glassware (Pyrex), an analytical balance, a blender, a mortar and pestle, a hotplate, a viscometer, a pycnometer (ISO LAB), a 40-mesh flour sieve, a metal spatula, a horn spoon, and parchment paper.

The materials used in this study were hemicellulose extracted from OPEFB (*Elaeis guineensis* Jacq.), NaOH (Merck), ethanol (Merck), sodium carboxymethylcellulose (CMC-Na), talc, glycerin (PT. Asih Utama), methylparaben (Gujarat Organics LTD), simple syrup, and distilled water.

The hemicellulose from oil palm empty fruit bunches (OPEFB) used as a suspending agent in this study was prepared using a modified method described by Miswanda et al. (20). Initially, 5,000 g of OPEFB, obtained from the residual production of a palm oil mill, were wet-sorted and washed with running water. The OPEFB fibers were then cut and dried in a drying cabinet at 50°C. The dried coarse fibers were ground using a grinding machine and sieved through a 100-mesh sieve to obtain OPEFB powder.

Preparation of Suspension from OPEFB Hemicellulose

Sodium carboxymethylcellulose (CMC-Na) and hemicellulose derived from oil palm empty fruit bunches (OPEFB) were ground using a

mortar and pestle until homogeneous, then dissolved in hot water to form a mucilage. Subsequently, glycerin was added to the materials intended for suspension preparation and ground until fully wetted and homogeneous. The mixture of suspension materials and glycerin was gradually added to the CMC-Na and OPEFB hemicellulose solution while continuously grinding to ensure homogeneity. The resulting mixture was transferred to a measuring cylinder along with rinse water from the mortar, followed by the addition of simple syrup. Finally, distilled water was added to adjust the volume to 100 ml. The suspension formula prepared in this study is presented in Table 1.

Table 1. Suspension formulation of OPEFB hemicellulose

Ingredient	Function	F0	F1	F2	F3	F4	F5
Talk	Additive	2.5	2.5	2.5	2.5	2.5	2.5
Hemicellulose of OPEFB	Suspending agent	-	1	-	1	-	2
CMC-Na	Suspending agent	-	-	1	-	2	1
Glycerin	Wetting agent	10	10	10	10	10	10
Methyl Paraben	Preservative	0.1	0.1	0.1	0.1	0.1	0.1
Simple Syrup	Sweetener	10	10	10	10	10	10
Distilled Water	Solvent	ad 100	ad 100	ad 100	ad 100	ad 100	ad 100

Evaluation of Suspension Formulation

Organoleptic Evaluation

From the first to the seventh day, organoleptic testing of the suspension formulation was conducted by assessing characteristics such as changes in color, odor, and taste.

pH Testing

A pH indicator strip, with its colored portion immersed in the suspension mixture, was used to determine the pH. The resulting color change was observed and compared to the pH scale provided on the pH strip packaging.

Density Testing

A sterile pycnometer was used to measure density. The empty pycnometer was weighed to determine its mass (a). The pycnometer was then filled with distilled water and weighed to obtain its mass (b). After drying and cleaning the pycnometer, the suspension formulation was added, and the pycnometer was weighed again to determine its mass (c). The density of the suspension was calculated using the following equation:

$$Density = \frac{(c-a)}{(b-a)} \quad (1)$$

Viscosity Testing

A Brookfield viscometer set at 30 rpm was used to measure the viscosity of the suspension.

Sedimentation Volume Testing

The suspension was stored under dark conditions and controlled temperature. The initial volume of the filled suspension (V_0) was recorded. Each day, without stirring, changes in the sedimentation volume were observed and recorded until a constant sedimentation level was achieved. The final sedimentation volume (Vu) was noted. The sedimentation volume was calculated using the following equation:

$$F = Vu / Vo \quad (2)$$

Redispersibility Testing

A 100 ml measuring cylinder containing the suspension was inverted and then returned to its original position. The number of inversions required to fully redisperse and resuspend the sedimented active components was used to evaluate the formulation. A redispersibility score of 100% indicates complete dispersion of the suspension. The redispersibility value decreases by 5% for each redispersibility test performed on identical samples.

Result and Discussion

Organoleptic Evaluation of Suspension Formulations

The organoleptic evaluation was conducted to observe the physical characteristics of the suspension formulations, including color, odor, and taste, over seven days of storage (Day 1, Day 3, and Day 7). This assessment aimed to determine the physical stability and acceptability of the suspensions containing hemicellulose extracted from oil palm empty fruit bunches (OPEFB) as a natural suspending agent. Table 2 shows the organoleptic test results.

Tabel 2. Organoleptic evaluation test of Suspension Formulation

No	Formula	Parameter	Day 1	Day 3	Day 7
1	F0	Color	Clear ↓ white	Clear ↓ white	Clear ↓ white
		Odor	Characteristic	Characteristic	Characteristic
		Taste	Sweet	Sweet	Sweet
2	F1	Color	White ↓ white	White ↓ white	White ↓ white
		Odor	Characteristic	Characteristic	Characteristic
		Taste	Sweet	Sweet	Sweet
3	F2	Color	Brown ↓ dark brown	Brown ↓ dark brown	Brown ↓ dark brown
		Odor	Characteristic	Characteristic	Characteristic
		Taste	Sweet	Sweet	Sweet
4	F3	Color	Brown ↓ dark brown	Brown ↓ dark brown	Brown ↓ dark brown
		Odor	Characteristic	Characteristic	Characteristic
		Taste	Sweet	Sweet	Sweet
5	F4	Color	Milky brown ↓ dark brown	Milky brown ↓ dark brown	Light cream ↓ dark brown
		Odor	Characteristic	Characteristic	Characteristic
		Taste	Sweet	Sweet	Sweet
6	F5	Color	Brown ↓ dark brown	Brown ↓ dark brown	Brown ↓ dark brown
		Odor	Characteristic	Characteristic	Characteristic
		Taste	Sweet	Sweet	Sweet

In terms of color, variations were observed among formulations depending on the type and concentration of suspending agents. Formula F0 (without a suspending agent) showed a clear to slightly whitish appearance throughout the observation period, indicating the absence of colored solid components. Formula F1, which contained 1% OPEFB hemicellulose, appeared white and remained relatively stable over time, suggesting that hemicellulose at low concentrations did not significantly influence the color of the suspension. In contrast, formulations F2 to F5 exhibited a brownish color that gradually darkened during storage. This coloration originated from the inherent brown pigment of OPEFB hemicellulose, which may still contain residual lignin and phenolic compounds after the isolation process. Notably, F4 (1% hemicellulose and 2% CMC-Na) displayed a lighter "milky brown" to cream hue, likely due to the dilution effect of CMC-Na, which is translucent and whitish in nature. Overall, no drastic discoloration occurred during storage, indicating good color stability of the suspensions.

Regarding odor, all formulations maintained a distinctive characteristic smell throughout the seven-day observation. This natural odor derived from plant-based hemicellulose did not change, implying the absence of degradation or microbial contamination during the storage period. The consistent odor profile suggests that the suspensions were chemically and microbiologically stable under the given conditions.

In terms of taste, all formulations consistently exhibited a sweet flavor throughout the observation period. The sweetness was attributed to the presence of Sirupus simplex used as a sweetening agent. No unpleasant or off-tastes were reported, indicating that the incorporation of OPEFB hemicellulose did not interfere with the organoleptic acceptability of the formulation. This demonstrates that the natural polysaccharide component is compatible with other excipients and does not negatively affect taste perception.

The organoleptic evaluation revealed that suspension formulations containing OPEFB-derived hemicellulose showed satisfactory

physical stability and sensory acceptability during storage. The only notable variation was in color intensity, which correlated with the concentration of hemicellulose used. These findings confirm that OPEFB hemicellulose can serve as a natural, stable, and safe suspending agent, providing a sustainable alternative to synthetic excipients in pharmaceutical suspensions.

pH of Suspension Formulation

The pH evaluation of the suspension formulations containing a combination of OPEFB hemicellulose and CMC-Na was conducted over a seven-day observation period to assess chemical stability and suitability for pharmaceutical use. On the first day, the measured pH value was approximately 8, which is higher than the ideal pH range for oral suspensions (5–7). This initial alkalinity may be attributed to residual alkaline components from the hemicellulose isolation process, as sodium hydroxide (NaOH) is commonly used during extraction and may leave trace amounts that influence the initial pH of the formulation.

By the third day, the pH of the suspension decreased to 7, indicating a gradual neutralization process. This change could be related to the interaction between the suspending agents (hemicellulose and CMC-Na) and other formulation components such as glycerin, methyl paraben, and the aqueous medium, which may facilitate the buffering effect or partial neutralization of residual alkaline groups.

After seven days of storage, the pH further decreased to 6, placing it within the ideal range for pharmaceutical suspensions (5–7). Maintaining the pH within this range is crucial for ensuring the stability of the active ingredients, preventing microbial growth, and maintaining the integrity of excipients. The observed pH adjustment over time suggests that the formulation gradually reached equilibrium, leading to a more stable system suitable for oral administration. These results indicate that the combination of OPEFB hemicellulose and CMC-Na as suspending agents can achieve an acceptable pH balance after a short stabilization period. The final pH stability within the optimal range supports the potential of OPEFB hemicellulose as a biocompatible and sustainable suspending agent, compatible with other excipients in pharmaceutical suspension formulations.

Density of Suspension Formulation

The density of the suspension formulations was determined using a pycnometer to evaluate the effect of varying concentrations of OPEFB hemicellulose and CMC-Na on the physical characteristics of the suspension system. As shown in Table 3, the pycnometer weight and calculated density values increased gradually from formula F0 to F5, ranging from 1.048 g/mL to 1.078 g/mL.

Tabel 3. Density of Suspension Formulation

No	Formula	Pycnometer Weight (g)	Density (g/mL)
1	F0	27.9746	1.048
2	F1	28.0544	1.056
3	F2	28.1447	1.069
4	F3	28.2154	1.071
5	F4	28.2504	1.075
6	F5	28.2824	1.078

This gradual increase in density indicates that the incorporation of higher concentrations of suspending agents, particularly OPEFB hemicellulose and CMC-Na, contributes to an increase in the overall viscosity and solid content of the suspension. The higher density values reflect a more compact particle arrangement and improved dispersion stability, which are desirable characteristics for pharmaceutical suspensions.

According to general formulation principles, an effective air-suspension carrier should have a density greater than 1.00 g/mL to ensure adequate sedimentation control and uniform particle distribution. All formulations in this study met this requirement, confirming that both OPEFB hemicellulose and CMC-Na can enhance the density of the suspension without

negatively affecting its homogeneity or flow properties. The results demonstrate that all tested formulations fulfilled the criteria for an effective air-suspension carrier, particularly by maintaining a density above 1.00 g/mL. This finding supports the potential of OPEFB-derived hemicellulose as a functional and sustainable suspending agent capable of improving the physical stability of pharmaceutical suspensions.

Viscosity of Suspension Formulation

Viscosity is an important parameter in evaluating the physical stability and flow behavior of pharmaceutical suspensions. It influences the sedimentation rate of dispersed particles and ensures uniform distribution during administration. The viscosity of the suspension formulations was measured using a Brookfield viscometer at 30 rpm, with the results presented in Table 4.

Table 4. Viscosity of Suspension Formulations

No	Formula	Spindle Number	Viscosity at 30 rpm (cP)
1	F0	4	-42.041
2	F1	4	110.5
3	F2	4	84.24
4	F3	4	186.4
5	F4	4	683.5
6	F5	4	622.1

The data indicate a clear increase in viscosity with the addition and concentration increase of OPEFB hemicellulose and CMC-Na as suspending agents. Formula F0 (without suspending agents) showed an anomalous negative reading (-42.041 cP), suggesting that the formulation lacked sufficient consistency for accurate viscosity measurement, likely due to the absence of thickening agents. In contrast, all other formulations (F1–F5) exhibited positive viscosity values, ranging from 84.24 cP to 683.5 cP, confirming that the inclusion of polymeric suspending agents significantly enhanced the internal resistance of the suspension system.

Among the tested formulations, F4 (1% hemicellulose and 2% CMC-Na) showed the highest viscosity value (683.5 cP), followed closely by F5 (2% hemicellulose and 1% CMC-Na) at 622.1 cP. These results indicate a synergistic effect between hemicellulose and CMC-Na in increasing viscosity and improving the rheological behavior of the suspension. The higher polymer concentration likely promotes the formation of a more extensive hydrogen-bonded network within the dispersion medium, enhancing particle suspension and reducing sedimentation.

Formulations with moderate viscosity values (F1–F3) remained pourable and stable, suggesting that the suspending agents provided adequate stability without compromising ease of administration. Excessively high viscosity can hinder redispersion and dosing accuracy; therefore, F4 and F5, while stable, may require optimization to balance flowability and sedimentation control.

Overall, the results demonstrate that the combination of OPEFB hemicellulose and CMC-Na effectively increases suspension viscosity, contributing to better physical stability. All formulations containing these agents exhibited rheological properties suitable for pharmaceutical suspensions, supporting the potential application of OPEFB hemicellulose as a natural and sustainable suspending agent in combination with conventional polymers.

Sedimentation Volume of Suspension Formulations

The sedimentation volume (F) is a key indicator of the physical stability of suspensions, reflecting the ability of a suspending agent to maintain dispersed particles within the continuous phase over time. A higher sedimentation volume indicates greater suspension stability and better redispersibility after settling.

As shown in Table 5, sedimentation volumes varied across formulations, depending on the type and concentration of suspending agents used. The control formulation (F0), which did not contain any suspending agent, exhibited

a very low and constant sedimentation volume (F = 0.02) throughout the seven-day observation period. This indicates rapid and irreversible sedimentation due to the absence of stabilizing polymers that could maintain particle dispersion.

The introduction of OPEFB hemicellulose in F1 slightly improved sedimentation stability (F = 0.03), suggesting that hemicellulose provided some degree of viscosity and particle suspension. However, the most notable improvement occurred in formulations F2 to F5, which contained combinations of OPEFB hemicellulose and CMC-Na. These formulations demonstrated significantly higher sedimentation volumes over time, with values ranging from 0.07 to 0.22 by Day 7.

The increase in sedimentation volume in these formulations can be attributed to the synergistic thickening effect of the two polysaccharides, which enhances viscosity and forms a more structured network within the suspension medium. Among all formulations, F5 exhibited the highest sedimentation volume (0.22 on Day 7), indicating optimal stability and minimal particle settling during storage. The gradual increase in sedimentation volume over the observation period also suggests that the suspensions reached a more stable equilibrium state, maintaining good redispersibility upon shaking.

According to the general requirements for pharmaceutical suspensions, formulations with sedimentation volumes above 0.1 are considered to possess acceptable physical stability. Therefore, all formulations containing hemicellulose and CMC-Na met this criterion. The results demonstrate that the combination of OPEFB hemicellulose and CMC-Na effectively enhances the sedimentation stability of the suspension. The synergistic interaction between these natural and synthetic polymers contributes to improved viscosity, reduced sedimentation rate, and greater uniformity of the dispersed phase, confirming their potential as efficient and sustainable suspending agents in pharmaceutical suspension formulations.

Table 5. Sedimentation Volume of Suspension Formulations

No	Formula	Sediment Volume (mL)			F (Sedimentation Ratio)		
		Day 1	Day 3	Day 7	Day 1	Day 3	Day 7
1	F0	2	2	2	0.02	0.02	0.02
2	F1	3	3	3	0.03	0.03	0.03
3	F2	11	12	19	0.11	0.12	0.19
4	F3	7	9	17	0.07	0.09	0.17
5	F4	0	17	20	0	0.17	0.2
6	F5	15	17	22	0.15	0.17	0.22

Redispersibility of Suspension Formulations

Redispersibility is a crucial parameter that reflects the ease with which a suspension can be rehomogenized after standing. A good pharmaceutical suspension should be easily redispersed with minimal agitation, ensuring uniform distribution of active ingredients before administration.

Table 6. Redispersibility of Suspension Formulations

No	Formula	Redispersibility (%)
1	F0	45
2	F1	80
3	F2	90
4	F3	90
5	F4	50
6	F5	50

As shown in Table 6, the redispersibility of the formulations varied significantly depending on the concentration and combination of suspending agents. The control formulation (F0), which lacked a suspending agent, showed the lowest redispersibility value (45%), indicating that the particles settled firmly at the bottom and were difficult to redisperse.

The addition of OPEFB hemicellulose in F1 improved redispersibility to 80%, demonstrating that hemicellulose contributed to enhanced viscosity and prevented hard sediment formation. The most favorable results were observed in F2 and F3, both achieving 90% redispersibility. These formulations contained balanced combinations of OPEFB hemicellulose and CMC-Na, suggesting a synergistic effect between the

two polymers. The interaction between hemicellulose and CMC-Na likely increased the suspension's structural viscosity, allowing particles to remain uniformly dispersed and easily resuspended after settling.

However, F4 and F5 exhibited reduced redispersibility (50%) despite their high viscosity values observed in previous measurements. This decrease could be attributed to the excessively high polymer concentration, which increased the internal resistance of the suspension and caused the formation of a dense sediment that required more energy to redisperse. Therefore, while high viscosity can enhance sedimentation stability, it may also negatively affect redispersibility if it becomes too pronounced. The results indicate that formulations F2 and F3 demonstrated the most optimal redispersibility behavior, balancing viscosity and suspension stability. These findings confirm that the combination of OPEFB hemicellulose and CMC-Na in appropriate ratios provides a synergistic effect, improving both suspension uniformity and ease of redispersion. Thus, OPEFB-derived hemicellulose shows strong potential as a natural, eco-friendly suspending agent suitable for stable and easily redispersible pharmaceutical suspensions.

Hemicellulose extracted from oil palm empty fruit bunches (OPEFB) demonstrated strong potential as a natural and sustainable suspending agent in pharmaceutical suspensions. When combined with sodium carboxymethyl cellulose (CMC-Na), OPEFB hemicellulose improved key formulation parameters, including viscosity, sedimentation stability, and redispersibility, without compromising organoleptic or pH characteristics. The formulations containing both polymers (F2 and F3) showed optimal performance, with stable pH values (5–7), acceptable density (>1.00 g/mL), balanced viscosity, sedimentation volume up to 0.22, and redispersibility reaching 90%. These results indicate a synergistic interaction between OPEFB hemicellulose and CMC-Na, enhancing the suspension's physical stability and uniformity. The study confirms that OPEFB-derived hemicellulose can serve as an effective, biodegradable, and eco-friendly alternative to synthetic suspending agents, supporting the development of more sustainable pharmaceutical formulations.

Conclusion

The findings of this study demonstrate that hemicellulose extracted from oil palm empty fruit bunches (OPEFB) possesses desirable characteristics as a natural suspending agent for pharmaceutical suspensions. The combination of OPEFB hemicellulose with sodium carboxymethyl cellulose (CMC-Na) produced formulations with optimal viscosity, stable pH (5–7), suitable density (>1.00 g/mL), and excellent sedimentation and redispersibility profiles. Among all formulations, F2 and F3 showed the best overall performance, indicating a synergistic effect between the two polymers in enhancing suspension stability and uniformity.

Therefore, OPEFB-derived hemicellulose can be considered a promising, biodegradable, and eco-friendly alternative to synthetic suspending agents, contributing to the sustainable utilization of palm oil waste in pharmaceutical applications. Future studies are recommended to explore its compatibility with active ingredients and evaluate long-term storage stability to support its broader use in green pharmaceutical formulation development.

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