

Formulation and Evaluation of a Chitooligosaccharide Peel-Off Gel Mask for Anti-Acne Activity Against *Propionibacterium acnes*

Elsa Fitria Apriani^{1*}, Miksusanti², Vitri Agustiarini³, Annisa Amriani⁴, Adik Ahmadi⁵, Maysa Yulianti⁶

^{1,2,3,4,5,6} Department of Pharmacy, Faculty of Mathematics and Natural Sciences, Sriwijaya University, Palembang-Prabumulih Road, KM 32 Indralaya, Ogan Ilir, South Sumatra, Indonesia

* Corresponding Author. Email: elsa.fitria@mipa.unsri.ac.id

ABSTRACT

Acne vulgaris is an inflammatory skin condition primarily caused by *Propionibacterium acnes* (*P. acnes*), which can lead to physical and psychological effects. Chitooligosaccharide (COS), a chitosan-derived oligosaccharide, possesses antibacterial and film-forming properties, making it a promising candidate for topical anti-acne formulations. This study aimed to formulate and evaluate the physical characteristics and antibacterial activity of a COS-based peel-off gel mask against *P. acnes*. Three formulas were prepared using COS concentrations of 0.25% (F1), 0.5% (F2), and 0.75% (F3). Evaluation parameters included organoleptic properties, homogeneity, pH, viscosity, spreadability, adhesiveness, drying time, and stability. Antibacterial activity was assessed using diffusion and dilution methods to determine the inhibition zone diameter, minimum inhibitory concentration (MIC), and minimum bactericidal concentration (MBC). Among the three formulas, F3 demonstrated the most optimal physical properties – clear, homogeneous, pH 6.50 ± 0.10 , viscosity $3,595.43 \pm 136.55$ cps, spreadability 5.00 ± 0.10 cm, adhesiveness 6.60 ± 0.10 s, and drying time 18.30 ± 0.10 min – without any phase separation. F3 also exhibited strong antibacterial activity with a 21.67 ± 1.65 mm inhibition zone, comparable to the positive control ($p > 0.05$). MIC and MBC values for F3 were determined to be 1250 ppm and 2500 ppm, respectively. These findings suggest that COS at 0.75% concentration is effective in a peel-off gel mask formulation with favorable physical stability and strong antibacterial efficacy against *P. acnes*, supporting its potential as a natural-based anti-acne treatment.

Copyright © 2025 Jsscr. All rights reserved.

Keywords:

Chitooligosaccharide; Peel-off gel mask; *Propionibacterium acnes*; Antibacterial activity; MIC, MBC

Received:
2025 -05-14

Accepted:
2025-07-28

Online:
2025 -07-30

1. Introduction

Acne (*acne vulgaris*) is a dermatological condition that affects approximately 9.4% of adolescents and young adults globally, often persisting into adulthood and exerting significant social and psychological impact [1]. It is primarily characterized by skin inflammation induced by *Propionibacterium acnes* (*P. acnes*), a gram-positive anaerobic bacterium involved in acne pathogenesis through several mechanisms. *P. acnes* promotes inflammation by increasing the production of IL-1 β , IL-8, and TNF- α [2], and secretes virulence factors such as proteases and lipases, which hydrolyze sebum triglycerides into irritative free fatty acids that exacerbate inflammation [3]. Additionally, *P. acnes* adheres to skin follicles and forms biofilms, making it more resistant to antimicrobial agents and prolonging the inflammatory response [4].

Various acne therapies are available, ranging from topical to systemic agents. However, the effectiveness of some antibacterial therapies is increasingly challenged by undesirable side effects and the growing potential for bacterial resistance. These limitations have encouraged the development of safer, natural, and more effective alternatives.

Chitooligosaccharide (COS), a natural polysaccharide derived from chitosan through depolymerisation, features a 1,4 β -glucosamine linkage [5]. COS has demonstrated multiple biological activities, including antibacterial, anti-inflammatory, and antioxidant properties [6]. El-Sayed et al. [7] showed that COS effectively inhibited *Bacillus cereus*, *Pseudomonas aeruginosa*, and *Candida albicans* with MIC values of 420 ppm, 1670 ppm, and 110 ppm, respectively. Furthermore, COS-modified bacterial cellulose membranes inhibited *Staphylococcus aureus* and *Escherichia coli* growth by $99.64 \pm 0.18\%$ and $90.56 \pm 0.06\%$, respectively [8]. Fernandes et al. [9] also demonstrated strong antibacterial activity at a 0.5% COS concentration. The antibacterial action of COS is attributed to its positively charged amine groups, which interact with negatively charged bacterial membranes, increasing permeability and ultimately causing cell death [10].

Peel-off gel masks have gained popularity in topical dermatological formulations, particularly for acne treatment, due to their occlusive film-forming properties that enhance stratum corneum hydration and facilitate active ingredient penetration [11],[12]. These formulations typically consist of a polymer and a plasticiser. In this study, hydroxypropyl methylcellulose (HPMC) was used as the gelling agent for its ability to produce clear gels with stable viscosity and efficient drug release [13], while polyvinyl alcohol (PVA) was employed as the plasticiser due to its adhesive and film-forming properties that aid in removing dead skin cells and impurities [14].

Although COS's antibacterial potential and the advantages of peel-off masks are well recognized, the formulation and comprehensive evaluation of a COS-based peel-off gel mask specifically targeting *P. acnes* has not been extensively reported. Therefore, this study aims to formulate and evaluate the physical characteristics and in vitro antibacterial activity of a chitooligosaccharide-based peel-off gel mask as a potential natural anti-acne treatment.

2. Methods

Materials

The materials used in this study included chitooligosaccharide (Xi'an Pincredit Bio-Tech Co., Ltd), polyvinyl alcohol (PVA, Bratachem®), hydroxypropyl methylcellulose (HPMC), glycerin, methylparaben (Bratachem®), propylparaben (Bratachem®), butylhydroxytoluene (BHT, Bratachem®), distilled water, clindamycin gel, a commercial comparator preparation, *Propionibacterium acnes* culture, Nutrient Agar (NA, Merck®), 0.5 McFarland turbidity standard, dimethyl sulfoxide (Bratachem®), Nutrient Broth (NB, Merck®), and sodium chloride (Sigma Aldrich®).

Preparation of Chitooligosaccharide Peel-Off Gel Mask

The peel-off gel mask was formulated into three variations based on chitooligosaccharide concentration: F1 (0.25%), F2 (0.5%), and F3 (0.75%). The complete composition of each formulation is presented in **Table 1**. The formulation design was adapted from Apriani et al. [15], while the selected COS concentrations were based on the antibacterial activity reported by Fernandes et al. [9].

The preparation process began by dissolving PVA in distilled water and stirring it with a magnetic stirrer at 60°C for 24 hours until a clear and homogeneous solution was obtained. In a separate container, HPMC was dispersed in hot water, stirred until smooth, and allowed to hydrate for 30 minutes. COS was mixed with glycerin until homogeneous, then incorporated into the combined base of PVA and HPMC. Subsequently, BHT, methylparaben, and propylparaben were added, and the mixture was adjusted to a final volume of 100 mL using distilled water.

Table 1. Composition of Chitoooligosaccharide Peel-Off Gel Mask Formulations

Ingredient	Function	F1 (% w/w)	F2 (% w/w)	F3 (% w/w)
Chitoooligosaccharide	Antibacterial	0.25	0.50	0.75
HPMC	Gelling agent	1.00	1.00	1.00
PVA	Film-forming agent (Plasticiser)	12.00	12.00	12.00
Glycerin	Humectant	5.00	5.00	5.00
BHT	Antioxidant	0.10	0.10	0.10
Methylparaben	Preservative	0.18	0.18	0.18
Propylparaben	Preservative	0.02	0.02	0.02
Distilled Water (ad)	Solvent	q.s. to 100	q.s. to 100	q.s. to 100

Evaluation of Physical Properties

The physical properties assessed included organoleptic characteristics, homogeneity, pH, viscosity, adhesiveness, spreadability, drying time, and stability. Organoleptic tests involved visual observation of texture, clarity, and odour. Homogeneity was evaluated by spreading the sample between two glass slides to assess uniformity. pH was measured using a calibrated pH meter. Viscosity was determined using a Brookfield viscometer (spindle no. 2, 30 rpm). Adhesiveness was measured by applying 0.25 g of sample between two glass plates under a 1 kg load, followed by an additional 80 g, with the detachment time recorded. Spreadability was measured by placing 0.5 g of the sample between glass plates and applying a 125 g weight for one minute, then measuring the spread diameter. Drying time was determined by applying the sample to a glass plate and recording the time required to form a dry film [16].

Physical Stability Testing

Stability tests were conducted using two methods: centrifugation and cycling tests. For centrifugation, the samples were spun at 5000 rpm for 30 minutes to evaluate phase separation. The cycling test involved subjecting samples to six temperature cycles: alternating storage at $5 \pm 3^\circ\text{C}$ and $40 \pm 2^\circ\text{C}$ for 24 hours each. Observations were made for organoleptic changes and pH variations before and after testing [17,18].

Inhibition Zone Diameter Test

Antibacterial activity was evaluated using the diffusion method. The test samples included the three COS gel mask formulations (F1-F3), clindamycin gel (positive control), the gel base (negative control), and a commercial market preparation. A bacterial suspension of *P. acnes* was cultured using the pour plate method. After the agar solidified, 6 mm wells were made and filled with 5 g of each preparation. The plates were incubated at 37°C for 5 × 24 hours, and the diameters of the inhibition zones were measured [19].

Determination of MIC and MBC

The MIC test was conducted by serial dilution using Nutrient Broth with COS concentrations ranging from 2500 ppm to 78.125 ppm. The MIC value was defined as the lowest concentration that produced no turbidity. For the MBC test, aliquots from the MIC test tubes were spread on Nutrient Agar plates inoculated with *P. acnes*. The MBC was determined as the lowest concentration that showed no bacterial growth after incubation [20].

Data Analysis

Data from the physical evaluation and antibacterial tests were analysed using SPSS for Windows v.22. The Shapiro-Wilk test was used to assess normality (significance level: 0.05). If the data were normally distributed ($p > 0.05$), one-way ANOVA was used; otherwise, the Kruskal-Wallis test was applied.

3. Results and Discussion

Physical Characteristics of Peel-Off Gel Mask

The physical properties of the chitoooligosaccharide (COS) peel-off gel mask formulations – F1 (0.25%), F2 (0.5%), and F3 (0.75%) – were evaluated based on visual appearance, homogeneity, pH, viscosity, spreadability, adhesiveness, and drying time, as summarized in **Table 2**. All three formulations exhibited acceptable physical characteristics for topical application.

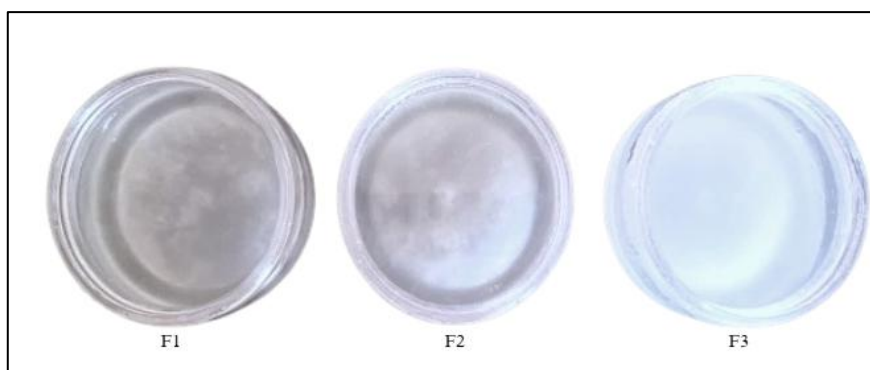


Figure 1. Visual comparison of F1–F3 peel-off gel mask formulations based on organoleptic observations

Figure 1 shows a visual comparison of the gel masks, indicating that each formula was clear, odorless, and uniformly thick in consistency. No visible particulate matter or phase separation was observed, suggesting good miscibility and polymer compatibility across all formulations. The appearance remained visually appealing, a critical factor for consumer acceptability in cosmetic formulations.

Quantitative analysis (**Table 2**) revealed that pH values increased with higher COS concentrations, ranging from 6.20 ± 0.10 in F1 to 6.50 ± 0.10 in F3. This trend is consistent with COS's mildly basic nature due to the presence of amino groups, which increase hydroxide ion availability upon dissolution [21],[22],[23]. All pH values remained within the dermatologically acceptable range of 4.5–6.5, thus posing minimal irritation risk.

Viscosity measurements also increased proportionally with COS content, from $2,496.20 \pm 89.15$ cps in F1 to $3,595.43 \pm 136.55$ cps in F3. The denser polymer network at higher COS concentrations may enhance the film-forming ability and occlusivity of the

mask [24],[25]. Spreadability showed an inverse relationship, decreasing from 6.40 ± 0.10 cm (F1) to 5.00 ± 0.10 cm (F3), which may result from increased viscosity limiting lateral gel flow during application.

Table 2. Evaluation results of physical characteristics of peel-off gel mask formulations (F1–F3)

Testing Parameter	F1	F2	F3
Organoleptic	Thick, odourless, and clear	Thick, odourless, and clear	Thick, odourless, and clear
Homogeneity	Homogeneous	Homogeneous	Homogeneous
pH	6.20 ± 0.10	6.30 ± 0.10	6.50 ± 0.10
Viscosity (cPs)	$2,496.20 \pm 89.15$	$2,823.08 \pm 136.18$	$3,595.43 \pm 136.55$
Spreadability (cm)	6.40 ± 0.10	5.40 ± 0.10	5.00 ± 0.10
Stickiness (s)	4.40 ± 0.10	4.50 ± 0.10	6.60 ± 0.10
Drying Time (min)	16.30 ± 0.10	17.30 ± 0.10	18.30 ± 0.10

Adhesiveness increased significantly with COS concentration, with F3 showing the highest stickiness value (6.60 ± 0.10 s), indicating better skin adhesion – a key feature for peel-off masks. Drying time also increased slightly from 16.30 ± 0.10 min in F1 to 18.30 ± 0.10 min in F3, which remains within acceptable limits for consumer use.

Statistical analysis revealed significant differences ($p < 0.05$) among formulations for all physical parameters, confirming that COS concentration strongly influences the gel's mechanical and sensory properties. Based on its optimal balance of clarity, viscosity, pH compatibility, adhesion, and film stability, F3 was selected as the best-performing formulation for further evaluation.

Stability Testing

The physical stability of the chitooligosaccharide peel-off gel mask formulations was assessed using centrifugation and cycling methods to simulate stress conditions during storage. The aim was to evaluate each formula's resilience against physical and environmental changes, such as phase separation and pH shift.

Table 3. Stability evaluation results of peel-off gel mask formulations before and after testing

Testing Parameter	Formula	Before	After
Organoleptic	F1	Clear, thick, and odourless	Clear, thick, and odourless
	F2	Clear, viscous, and odourless	Clear, viscous, and odourless
	F3	Clear, viscous, and odourless	Clear, viscous, and odourless
pH	F1	6.20 ± 0.10	6.10 ± 0.10
	F2	6.30 ± 0.10	6.20 ± 0.10
	F3	6.50 ± 0.10	6.30 ± 0.10
Homogeneity	F1	Homogeneous	Homogeneous

F2	Homogeneous	Homogeneous
F3	Homogeneous	Homogeneous

Centrifugation testing was performed at 5000 rpm for 30 minutes. None of the formulations (F1–F3) showed phase separation or sedimentation, indicating excellent physical stability under mechanical stress. In addition, the cycling test involved six alternating temperature cycles between $5 \pm 3^\circ\text{C}$ and $40 \pm 2^\circ\text{C}$ over 24-hour periods. Observations were made before and after testing for organoleptic changes, pH, and homogeneity.

As presented in **Table 3**, all three formulas remained clear, homogeneous, and odourless throughout the testing period, with no visible changes in texture or appearance. However, a slight reduction in pH was observed in each formulation after cycling. For instance, F3 exhibited a decrease in pH from 6.50 ± 0.10 to 6.30 ± 0.10 , though still within the skin-compatible range.

This pH shift is likely due to changes in ionic interactions and reversible hydrogen bonding influenced by temperature variation, as previously described by Wu et al. [26] and Liang et al. [27]. Despite these changes, the formulas maintained their structural and physicochemical integrity, confirming the formulations' short-term stability under simulated storage conditions.

Antibacterial Activity: Inhibition Zone Diameter

The antibacterial activity of the chito oligosaccharide (COS) peel-off gel mask formulations was evaluated using the agar diffusion method against *Propionibacterium acnes*. This test aimed to measure the diameter of the inhibition zone formed by each formula and compare it to positive and negative controls as well as a commercial product.

Table 4. Inhibition zone diameter of peel-off gel mask formulations against *P. acnes*

Formula	Inhibition Zone Diameter (mm) \pm SD	Antibacterial Strength Criteria (CLSI, 2014)
F1	$17,33 \pm 2,08^c$	Medium
F2	$17,33 \pm 1,53^c$	Medium
F3	21.67 ± 1.65^{ab}	Strong
Positive Control	$22,53 \pm 1,08^a$	Strong
Negative Control	0 ± 0^d	Weak
Commercial Comparator	19.00 ± 1.00^{bc}	Medium
Media Only	0 ± 0^d	Weak

Notes: Values followed by different lowercase letters in the same column indicate significant differences in the Duncan Post Hoc test ($p < 0.05$).

As shown in **Table 4**, Formula 3 (F3), which contained 0.75% COS, exhibited the strongest antibacterial activity with an inhibition zone diameter of 21.67 ± 1.65 mm. This value falls into the strong category of antibacterial efficacy, as per the Clinical and Laboratory Standards Institute (CLSI, 2014), which classifies inhibition zones above 20 mm as strong. F3's performance was not significantly different from the positive control (clindamycin gel, 22.53 ± 1.08 mm; $p > 0.05$), indicating comparable antibacterial potency.

Formulas F1 and F2, with lower COS concentrations of 0.25% and 0.5% respectively, both produced inhibition zones of 17.33 mm, classified as moderate antibacterial activity. Meanwhile, the commercial comparator exhibited a moderate zone of 19.00 ± 1.00 mm. The negative control (gel base) and blank media produced no inhibition zones (0 mm), confirming that the antibacterial effect originated from the active ingredients.

Statistical analysis using Duncan's post hoc test showed that F3 was significantly different ($p < 0.05$) from F1, F2, and the negative controls, but not from the positive control and comparator. These findings confirm that a COS concentration of 0.75% is optimal for achieving strong antibacterial activity against *P. acnes* in gel formulation.

MIC and MBC Determination

The antibacterial activity of the best-performing formula, F3 (containing 0.75% chitooligosaccharide), was further evaluated through Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC) tests using broth dilution and spread plate methods. These tests aimed to determine the lowest concentration of the formulation capable of inhibiting (MIC) and killing (MBC) *Propionibacterium acnes*.

As shown in **Table 5**, F3 exhibited an MIC value of 1250 ppm, indicated by the absence of turbidity in the broth medium at this concentration. This means that bacterial growth was successfully inhibited at 1250 ppm. The MBC value for F3 was found to be 2500 ppm, as evidenced by the absence of bacterial colonies on the nutrient agar plate after incubation, indicating complete bactericidal activity at this concentration.

Table 5. MIC and MBC results of F3 and comparator preparations against *Propionibacterium acnes*

Testing	Test Solution	<i>Propionibacterium acnes</i>					
		2500 ppm	1250 ppm	625 ppm	312.5 ppm	156.25 ppm	78.125 ppm
MIC	F3	-	-	+	+	+	+
	Comparator Preparations	-	+	+	+	+	+
MBC	F3	-	+	+	+	+	+
	Comparator Preparations	+	+	+	+	+	+

Note: (-) indicates no bacterial growth; (+) indicates bacterial growth observed

In contrast, the commercial comparator preparation demonstrated an MIC of 2500 ppm, but failed to exhibit any bactericidal effect within the tested concentration range, as bacterial growth was still observed at all levels during MBC testing. This result implies that while the comparator could inhibit bacterial proliferation at high concentration, it could not fully eliminate the bacteria even at 2500 ppm.

These findings suggest that F3 is more effective both in inhibiting and killing *P. acnes* at lower concentrations compared to the commercial product. The superior efficacy of F3 can be attributed to the cationic nature of chitooligosaccharide, which facilitates electrostatic interaction with the negatively charged bacterial membrane. This interaction disrupts membrane integrity, impairs nutrient transport, and ultimately leads to cell lysis [28]. Overall, the results confirm that the F3 formulation possesses strong concentration-dependent antibacterial activity and offers a promising alternative for anti-acne treatment.

While this study successfully demonstrated the antibacterial activity of chitooligosaccharide peel-off gel masks against *P. acnes* through inhibition zone, MIC, and MBC analysis, several limitations should be acknowledged. As an in vitro study, the results may not directly reflect in vivo biological responses, necessitating further validation in animal or human skin models. Additionally, only a single bacterial strain was tested, limiting the generalizability of findings to broader clinical or resistant strains. The mechanism of action was also not explored at the molecular level, which warrants further investigation to support its therapeutic development.

4. Conclusion

The physical characteristics of the peel-off gel mask formulations were significantly influenced by chitooligosaccharide (COS) concentration. An increase in COS content resulted in higher pH, viscosity, adhesiveness, and drying time, while decreasing spreadability. Among the three tested formulas, F3 (0.75% COS) demonstrated the most optimal performance, fulfilling the desired criteria for a topical gel preparation. F3 also exhibited good physical stability and strong antibacterial activity, with an inhibition zone of 21.67 ± 1.65 mm and MIC and MBC values of 1250 ppm and 2500 ppm, respectively. These results support the potential of COS-based peel-off gel masks as a promising natural anti-acne therapy. Future research is recommended to validate these findings through in vivo studies, extended stability testing, and broader evaluation against clinical or resistant strains of *P. acnes*.

Acknowledgments:

The authors would like to express their sincere gratitude to the Department of Pharmacy, Faculty of Mathematics and Natural Sciences, Sriwijaya University, for providing research facilities and administrative support. Appreciation is also extended to the laboratory staff who contributed to the technical execution of this study.

Conflicts of Interest:

The authors declare no conflicts of interest related to the conduct, authorship, or publication of this research.

References

- [1] D. L. Guguluş *et al.*, "The Epidemiology of Acne in the Current Era: Trends and Clinical Implications," *Cosmetics*, vol. 12, no. 3, pp. 106, 2025. [Online]. Available: <https://doi.org/10.3390/cosmetics12030106>
- [2] S. Ryu, H. M. Han, P. I. Song, C. A. Armstrong, and Y. Park, "Suppression of propionibacterium acnes infection and the associated inflammatory response by the antimicrobial peptide P5 in Mice," *PLoS One*, vol. 10, no. 7, pp. 1-18, 2015. [Online]. Available: <https://doi.org/10.1371/journal.pone.0132619>
- [3] V. Borrel *et al.*, "Adaptation of acneic and non acneic strains of Cutibacterium acnes to sebum-like environment," *Microbiologyopen*, vol. 8, no. 9, pp. 1-10, 2019. [Online]. Available: <https://doi.org/10.1002/mbo3.841>
- [4] K. I. Okuda *et al.*, "The composition and structure of biofilms developed by Propionibacterium acnes isolated from cardiac pacemaker devices," *Front. Microbiol.*, vol. 9, no. FEB, pp. 1-12, 2018. [Online]. Available: <https://doi.org/10.3389/fmicb.2018.00182>
- [5] Y. xia Mei, X. yi Dai, W. Yang, X. wei Xu, and Y. xiang Liang, "Antifungal activity of chitooligosaccharides against the dermatophyte Trichophyton rubrum," *Int. J. Biol. Macromol.*, vol. 77, pp. 330-335, 2015. [Online]. Available:

- <https://doi.org/10.1016/j.ijbiomac.2015.03.042>
- [6] L. Lillo, J. Alarcón, G. Cabello, C. Céspedes, and C. Caro, "Antibacterial activity of chitooligosaccharides," *Zeitschrift fur Naturforsch. - Sect. C J. Biosci.*, vol. 63, no. 9-10, pp. 644-648, 2008. [Online]. Available: <https://doi.org/10.1515/znc-2008-9-1005>
- [7] S. T. El-Sayed, A. M. Ali, and N. I. Omar, "A comparative evaluation of antimicrobial activity of chitooligosaccharides with broad spectrum antibiotics on growth of some pathogenic microorganisms," *Biocatal. Agric. Biotechnol.*, vol. 22, no. July, p. 101382, 2019. [Online]. Available: <https://doi.org/10.1016/j.bcab.2019.101382>
- [8] N. Yin, R. Du, F. Zhao, Y. Han, and Z. Zhou, "Characterization of antibacterial bacterial cellulose composite membranes modified with chitosan or chitooligosaccharide," *Carbohydr. Polym.*, vol. 229, no. October 2019, p. 115520, 2020. [Online]. Available: <https://doi.org/10.1016/j.carbpol.2019.115520>
- [9] J. C. Fernandes *et al.*, "Antimicrobial effects of chitosans and chitooligosaccharides, upon Staphylococcus aureus and Escherichia coli, in food model systems," *Food Microbiol.*, vol. 25, no. 7, pp. 922-928, 2008. [Online]. Available: <https://doi.org/10.1016/j.fm.2008.05.003>
- [10] J. Li and S. Zhuang, "Antibacterial activity of chitosan and its derivatives and their interaction mechanism with bacteria: Current state and perspectives," *Eur. Polym. J.*, vol. 138, no. August, p. 109984, 2020. [Online]. Available: <https://doi.org/10.1016/j.eurpolymj.2020.109984>
- [11] A. O. R. Beringhs, J. M. Rosa, H. K. Stulzer, R. M. Budal, and D. Sonaglio, "Green clay and aloe vera peel-off facial masks: Response surface methodology applied to the formulation design," *AAPS PharmSciTech*, vol. 14, no. 1, pp. 445-455, 2013. [Online]. Available: <https://doi.org/10.1208/s12249-013-9930-8>
- [12] L. Pratiwi and S. Wahdaningsih, "FORMULASI DAN AKTIVITAS ANTIOKSIDAN MASKER WAJAH GEL PEEL OFF EKSTRAK METANOL BUAH PEPAYA (Carica papaya L.)," *Jurnal Farmasi Medica*, vol. 1, no. 2, 2018. [Online]. Available: <https://doi.org/10.35799/pmj.1.2.2018.21643>
- [13] H. O. Akinosho and L. Wicker, "Stability of β -carotene loaded emulsions vary by viscosity of hydroxypropyl methylcellulose dispersions," *Lwt*, vol. 63, no. 1, pp. 582-589, 2015. [Online]. Available: <https://doi.org/10.1016/j.lwt.2015.02.024>
- [14] T. Raju, "Design, Formulation and Optimization of Peel-Off Face Mask Gel for the Symptomatic Treatment of Rosacea," *J. Pharm. Res. Sci. Technol.*, vol. 6, no. 2, pp. 96-104, 2022. [Online]. Available: <https://doi.org/10.31531/jprst.1000164>
- [15] E. F. Apriani, M. Miksusanti, N. Fransiska, E. Fitria, and A. M. Miksusanti, "Formulation And Optimization Peel-Off Gel Mask with Polyvinyl Alcohol and Gelatin Based Using Factorial Design from Banana Peel Flour (Musa paradisiaca L) As Antioxidant," *Indonesian Journal of Pharmacy*, vol. 32, no. 2, pp. 261-268, 2022. Available: <https://doi.org/10.22146/ijp.3408>
- [16] M. Miksusanti, E. F. Apriani, and N. Aprida, "Formulation and Optimization Peel-Off Gel Mask with Polyvinyl Alcohol and Whey Protein-Based using Factorial Design from Ethanolic Extract of Mangosteen Peel (Garcinia Mangostana) as Antioxidant," *Res. J. Pharm. Technol.*, vol. 16, no. 2, pp. 870-878, 2023. [Online]. Available: <https://doi.org/10.52711/0974-360X.2023.00148>
- [17] M. Mardiyanto, E. F. Apriani, and M. H. Alfarizi, "Formulation and In-vitro Antibacterial Activity of Gel containing Ethanolic extract of Purple Sweet Potato Leaves (Ipomoea batatas (L.) Loaded Poly Lactic Co-Glycolic Acid

- Submicroparticles against *Staphylococcus aureus*,” *Res. J. Pharm. Technol.*, vol. 15, no. 8, pp. 3599–3605, 2022. [Online]. Available: <https://doi.org/10.52711/0974-360X.2022.00603>
- [18] E. F. Apriani, S. Shiyan, D. Hardestyariki, and M. Febriani, “Factorial Design for the Optimization of Clindamycin HCl-Loaded Ethosome with various concentrations of Phospholipon 90g and Ethanol,” *Res. J. Pharm. Technol.*, vol. 16, no. 4, pp. 1561–1568, 2023. [Online]. Available: <https://doi.org/10.52711/0974-360X.2023.00255>
- [19] D. Dianasari, H. Hanifah, and N. Nuri, “Potensi Ekstrak dan Fraksi Buah Maja (*Aegle marmelos*) sebagai Agen Antibakteri terhadap *Propionibacterium acnes*,” *J. Sains dan Kesehat.*, vol. 4, no. 4, pp. 401–406, 2022. [Online]. Available: <https://doi.org/10.25026/jsk.v4i4.1290>
- [20] E. F. Apriani, Y. Rosana, and I. Iskandarsyah, “Formulation, characterization, and in vitro testing of azelaic acid ethosome-based cream against *Propionibacterium acnes* for the treatment of acne,” *J. Adv. Pharm. Technol. Res.*, vol. 10, no. 2, pp. 75–80, Apr. 2019. [Online]. Available: https://doi.org/10.4103/japtr.JAPTR_289_18
- [21] F. Coreta-Gomes *et al.*, “Contribution of non-ionic interactions on bile salt sequestration by chitooligosaccharides: Potential hypocholesterolemic activity,” *J. Colloid Interface Sci.*, vol. 646, no. 1, pp. 775–783, 2023. [Online]. Available: <https://doi.org/10.1016/j.jcis.2023.05.056>
- [22] L. Phil, M. Naveed, I. S. Mohammad, L. Bo, and D. Bin, “Chitooligosaccharide: An evaluation of physicochemical and biological properties with the proposition for determination of thermal degradation products,” *Biomed. Pharmacother.*, vol. 102, no. November 2017, pp. 438–451, 2018. [Online]. Available: <https://doi.org/10.1016/j.biopha.2018.03.108>
- [23] T. Anita Zaharah and J. H. Hadari Nawawi, “SINTESIS, KARAKTERISASI DAN APLIKASI KITOSAN DARI CANGKANG UDANG WANGKANG (*Penaeus orientalis*) SEBAGAI KOAGULAN DALAM MENURUNKAN KADAR BAHAN ORGANIK PADA AIR GAMBUT,” vol. 5, no. 3, pp. 52–59, 2016.
- [24] J. Luo, H. Yang, and T. Wen, “Experimental investigations on the influence of polymerization degree in polymer-assisted pool boiling enhancement,” *Int. Commun. Heat Mass Transf.*, vol. 142, p. 106650, 2023. [Online]. Available: <https://doi.org/10.1016/j.icheatmasstransfer.2023.106650>
- [25] A. B. Al-Odayni *et al.*, “Viscosity, degree of polymerization, water uptake, and water solubility studies on experimental dichloro-bisigma-based dental composites,” *Appl. Sci.*, vol. 11, no. 8, 2021. [Online]. Available: <https://doi.org/10.3390/app11083577>
- [26] Y. Wu, Y. Huang, Y. Zhou, X. Ren, and F. Yang, “Degradation of chitosan by swirling cavitation,” *Innov. Food Sci. Emerg. Technol.*, vol. 23, pp. 188–193, 2014. [Online]. Available: <https://doi.org/10.1016/j.ifset.2014.02.001>
- [27] S. Liang, Y. Sun, and X. Dai, “A review of the preparation, analysis and biological functions of chitooligosaccharide,” Aug. 01, 2018, MDPI AG. [Online]. Available: <https://doi.org/10.3390/ijms19082197>
- [28] A. B. Vishu Kumar, M. C. Varadaraj, L. R. Gowda, and R. N. Tharanathan, “Characterization of chito-oligosaccharides prepared by chitosanolsysis with the aid of papain and Pronase, and their bactericidal action against *Bacillus cereus* and *Escherichia coli*,” *Biochem. J.*, vol. 391, no. 2, pp. 167–175, 2005. [Online]. Available: <https://doi.org/10.1042/BJ20050093>
- [29] P. J. Wibawa *et al.*, “Green synthesized silver nanoparticles immobilized on

activated carbon nanoparticles: Antibacterial activity enhancement study and its application on textiles fabrics," *Molecules*, vol. 26, no. 13, 2021. [Online]. Available: <https://doi.org/10.3390/molecules26133790>