SYNTHESIS AND CHARACTERIZATION OF CURCUMIN-CHITOSAN LOADED GOLD NANOPARTICLES BY *Oryctes rhinoceros'* CHITIN FOR COSMECEUTICAL APPLICATION

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DEDICATION

"I am only one, but still, I am one. I cannot do everything, but still, I can do something and because I cannot do everything, I will not refuse to do the something that I can do."

I dedicate this thesis to my family for their endless support, affection, belief, and love. I would also like to dedicate this thesis to my supervisor for her guidance, support, and letting me do the things I am most comfortable with. To my friends, who have always brought sunshine during the darkest of times. They bring joy and comfort during those stressful moments. And the ultimate supporter, as a thousand times I have failed, but still your mercy remains. Thank you, Allah S.W.T

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ABSTRACT

A breakthrough in cosmeceuticals by utilizing insects as major ingredients in cosmetic products is gaining popularity. Therefore, the interest in rare sources of ingredients, for instance, from the *Oryctes rhinoceros* beetle, can bring huge benefit in turning pest to wealth. In this study, curcumin was chosen as the active ingredient loaded into chitosan-gold nanoparticles (CCG-NP). However, curcumin is unstable, and has high sensitivity to light thus curcumin has low bioavailability. Therefore, chitosan extracted from *O. rhinoceros* acts as a drug carrier to overcome these problems. In order to overcome the problems, several objectives were achieved, including optimizing the parameters of chitin extraction, deacetylation of chitosan, followed by characterization of *O. rhinoceros'* chitin and chitosan by their physical properties and spectrophotometer evaluation, to name a few. CCG-NPs are synthesized and characterized, and their efficacy is determined by their drug release profile, antimicrobial and anti-tyrosinase properties, and toxicity test. The best RSM chitin extraction parameters were 1 M NaOH, 99 °C, 20 ml/g of sample for deproteinization and 3.92 M HCl, 75 °C, 12 ml/g of sample for decalcification. Chitin and chitosan from *O. rhinoceros* are comparable to commercial chitin and chitosan. CCG-NPs are successfully synthesized at 70 °C for 60 minutes under optimal conditions of reactant ratio of 2:0.5 (0.5 mM $HAuCl_4$: 0.1 % curcumin). The shape of the CCG-NP is determined via FE-SEM, and it is round, and the size is 128.27 d.nm. The value of the zeta potential is 20.2 ± 3.81 mV showing a stable mixture. An *in vitro* drug release profile shows a cumulative drug release in 24 hours of 52.99 %. The zone diameter for inhibition for *E. coli* and *S. aureus* was 7.0 mm and 8.5 mm, respectively, with tyrosinase enzyme inhibition of 66.385 ± 3.0%. The cytotoxicity of cell viability IC_{50} is 58% of the CCG-NP concentration indicating a mild toxicity trait. To conclude, CCG-NP is a stable, spherical, nano-sized, homogeneous solution with a good drug release profile, antimicrobial properties, enhanced anti-tyrosinase activity, and is non-toxic for the cosmeceutical applications.

ABSTRAK

Penemuan baharu dalam kosmeseutikal dengan menggunakan serangga sebagai bahan utama dalam produk kosmetik menjadi semakin popular. Oleh itu, perhatian terhadap sumber bahan yang jarang ditemui, contohnya, daripada kumbang tanduk, *Oryctes rhinoceros*, boleh membawa manfaat yang besar dalam mengubah serangga perosak kepada sesuatu yang bernilai. Dalam kajian ini, kurkumin dipilih sebagai bahan aktif yang digabungkan bersama kitosan-nanozarah emas (CCG-NP). Walau bagaimanapun, kurkumin tidak stabil, serta mudah terurai justeru menyumbang kepada bioavailabiliti yang rendah. Oleh itu, kitosan yang diekstrak daripada *O. rhinoceros* bertindak sebagai '*drug carrier'* untuk mengatasi masalah tersebut. Bagi mengatasi masalah tersebut, beberapa objektif telah dicapai, termasuk mengoptimumkan parameter pengekstrakan kitin, penyahetilasi kitosan, diikuti dengan pencirian kitin dan kitosan *O. Rhinoceros*. CCG-NPs disintesis dan dicirikan, dan keberkesanannya ditentukan oleh profil pelepasan ubat, sifat antimikrob dan anti-tirosinase, serta ujian ketoksikan. Parameter pengekstrakan kitin RSM terbaik ialah 1 M NaOH, 99 °C, 20 ml/g sampel untuk penyahproteinan dan 3.92 M HCl, 75 °C, 12 ml/g sampel untuk penyahkalsifikasian. Kitin dan kitosan daripada *O. rhinoceros* adalah setanding dengan kitin dan kitosan komersial. CCG-NPs berjaya disintesis pada 70 °C selama 60 minit di bawah keadaan optimum nisbah 2:0.5 (0.5 mM $HAuCl_4$: 0.1% curcumin). Melalui FE-SEM, bentuk CCG-NP adalah sfera dengan saiz 128.27 d.nm . Nilai potensi zeta ialah 20.2 ± 3.81 mV menunjukkan sebatian yang stabil. Profil pelepasan ubat *in vitro* menunjukkan pelepasan ubat kumulatif dalam 24 jam sebanyak 52.99 %. Antimikrob untuk *E. coli* dan *S. aureus* ialah 7.0 mm dan 8.5 mm, masing-masing, dengan perencatan enzim tyrosinase sebanyak 66.385 ± 3.0%. Sitotoksisiti IC_{50} adalah sederhana dengan hanya 58 %. Sebagai kesimpulan, CCG-NP ialah larutan homogen yang stabil, berbentuk sfera, bersaiz nano, dengan profil pelepasan ubat yang baik, sifat antimikrob, aktiviti anti-tirosinase yang lebih efektif, dan tidak bertoksik untuk kegunaan kosmetik.

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LIST OF SYMBOLS AND ABBREVIATIONS

%	-	Percentage
^{0}C	-	Degree celsius
13CP/MAS-NMR	-	13C cross-polarization magic-angle-spinning nuclear magnetic resonance
1H-NMR	-	Proton nuclear magnetic resonance
ANOVA	-	Analysis of variance
$Ca(OH)_2$	-	Calcium hydroxide
CCG-NP	-	Curcumin-chitosan loaded gold nanoparticle
CH_3COOH	-	Acetic acid
DD	-	Degree of deacetylation
DMSO	-	Dimethyl sulfoxide
DSC	-	Differential scanning calorimetry
EDX	-	Energy dispersive x-ray
FE-SEM	-	Field emission scanning electron microscope
FTIR	-	Fourier-transform infrared spectroscopy
GlcNAc	-	1,4 linked N-acetylglucosamine
h	-	Hour
H_2O_2	-	Hydrogen peroxide
H_2SO_4	-	Sulphuric acid
HCl	-	Hydrochloric acid
HCOOH	-	Formic acid
HNO_3	-	Nitric acid
IC_{50}	-	The half-maximal inhibitory concentration
IR	-	Infrared
K_2CO_3	-	Potassium carbonate
$KMnO_4$	-	Potassium permanganate
KOH	-	Potassium hydroxide

M	-	Molarity
min	-	Minute
ml	-	Milliliter
mm	-	Millimeter
MTT	-	[3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide
N	-	Nomality
Na_2CO_3	-	Sodium carbonate
Na_2SO_4	-	Sodium sulphate
NaClO	-	Sodium hypochlorite
NaOH	-	Soidum hydroxide
nm	-	Nanometer
OD	-	Optical density
P_2O_5	-	Phosphorus pentoxide
RSM	-	Response surface methodology
SEM	-	Scanning electron microscopy
SO_2	-	Sulphur dioxide
SPR	-	Surface plasmon resonance
TGA	-	Thermogravimetric analysis
TPP	-	Tripolyphosphate
Tween-20	-	Polysorbate 20
Tween-80	-	Polysorbate 80
UTM	-	Universiti Teknologi Malaysia
UV-vis	-	Ultra-Violet visible spectrophotometer
w/v	-	Weight/volume
w/w	-	Weight/weight
WBC	-	Water binding capacity
WHO	-	World health organization
XRD	-	X-ray diffraction
α	-	Alpha
β	-	Beta
γ	-	Gamma
μl	-	Microliter

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LIST OF PUBLICATIONS

Journals:

(i) **N. Alyani Zainol Abidin**, F. Kormin, N. Akhma Zainol Abidin, N.A.F Mohamed Anuar, M.F. Abu Bakar (2020). "The potential of insects as alternative sources of chitin: An overview on the chemical method of extraction from various sources", International Journal of Molecular Sciences. Vol. 21, No. 14, pp. 4978.

(ii) **N.A. Zainol Abidin,** F. Kormin, N. Akhma Zainol Abidin, M.F. Abu Bakar, A.C. Iwansyah (2023). "Anti-tyrosinase activities of curcumin-chitosan gold nanoparticles synthesized from beetle (*Oryctes rhinoceros*)", Asian Journal of Chemistry. Vol. 35, No. 1, pp. 79-82.

LIST OF AWARDS

(i) **Silver medal in International Research and Innovation Symposium and Exposition 2022 (RISE2022):**

N. Alyani Zainol Abidin, F. Kormin, N. Akhma Zainol Abidin, "Synthesis and characterization of curcumin-chitosan loaded gold nanoparticles by *Oryctes rhinoceros'* chitin for cosmeceutical application."

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VITA

Nurul Alyani Binti Zainol Abidin is from Malaysia and was born on February 13th, 1994. She completed her bachelor's degree in science (Food Technology) with honours from Universiti Tun Hussein Onn Malaysia in 2017 with a great CGPA. She was offered a fast-track course for her doctorate studies at UTHM. Straightaway, she started her PhD in the same year she graduated with her bachelor's degree. The area of biopolymers has struck her fancy since then. She studied the extraction method for chitin and chitosan from a rare source, which was *O. rhinoceros,* a pest for oil palm trees. Continuing with the high potential of chitosan from the rhinoceros beetle, she continued to synthesis and characterise the chitosan-curcumin gold nanoparticles (CCG-NP). To support the claim stating that chitosan from pest had great value, she elucidated the cosmeceutical potential of the CCG-NP mixture through *in vitro* drug release, antimicrobial, and anti-tyrosinase studies. To completely determine that the mixture is safe for human contact, cytotoxicity for CCG-NP was studied as well. Throughout her PhD journey, she had completed, assisted, and participated in eight different grants, both internal and national. The fields involved were food science, nutrition, nanotechnology, product development, pharmacology, and nutraceuticals.