



An Insight into the Dermatological Application of Microencapsulated Neem and Castor oils in an Anti-Aging Cream

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ABSTRACT

Herbal oils and its formulas are in increasing demand in the cosmetic and pharmaceutical industry. The research paper highlights the potent anti-inflammatory, antioxidant, and antimicrobial capabilities of neem and castor oils. The objective of research work is to prepare oil-filled Microcapsules incorporated in a cream formulation. This formulation further subjected to analytical evaluation by sophisticated instrument. Microcapsule were prepared by ionic gelation process. The microcapsule containing cream was created using batches of varying concentrations, denoted as F1, F2, F3, F4 and F5. Further microcapsules morphology was studied by TGA, SEM, LE was calculated and FTIR was used to characterize manufactured microcapsules. As a part of biological study formulation was subjected for animal study and in vitro DPPH free radical scavenging assay. A variety of parameters, including pH, spreadability, homogeneity, and viscosity, were used to evaluate each composition. Formulations F4 and F5, according to the study, had good spreadability, homogeneity with a decent look, good consistency, a pH of 7, no phase separation, and were easy to get rid of. Further these batches namely F4 and F5 was tested for non-irritancy using animal study according to CPCSEA guidelines. These investigations imply that the cream of the F5 batch has a safer and more stable composition, that might result in a synergistic effect. The F5 batch was showing best formulation in order to prevent aging of the skin, it can be served as a barrier for shielding the skin.

Keywords: Anti-aging, Herbal cream, Microencapsulation, Essential oils.

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INTRODUCTION

The skin acts as a barrier, keeping the body secure from viruses and dehydration [1]. Nutrition, air pollution, exposure to the sun, and sleep deprivation all have an impact on skin aging. Photoaging or chronological changes cause the aging of the skin. Reactive oxygen species, which are produced continuously during oxidative cell metabolism, are the cause of these alterations.¹ The outermost layer which is epidermis if for the protecting skin that covers the body's surface and provides an infection barrier. Aging is brought on by thinning of this epidermal layer, loosening of collagen, and elastic fiber. Extrinsic variables like sun exposure, smoking, dietary intake, and pollution can also contribute to aging, as can intrinsically factors like heredity, cellular metabolism, hormones, and metabolic processes. [2] Continuous exposure to ultraviolet radiation from sunlight damages human beings' skin and contributes to the complex process of skin aging. Skin wrinkling eventually arises from collagen deficiency caused by reactive oxygen species created by ultraviolet light [3]. Artificial cream work rapidly on the skin. This chemical-based skin care products do offer benefits to the skin but they come with side effects. If you use them, you are actually exposing your skin to pollution and toxicity. Natural creams are earth friendly. Natural health and beauty product use natural ingredients that won't affect your body. Natural product work with your skin instead against it. [4]

Drug Profile:

Following oils are used in microencapsulation technique:

i. Neem Oil:

Biological name: *Azadirachta indica*

Chemical constituent: azadirachtin, nibolinin, nimbin, nimbidin, nimbidol.

Category: Anti-aging, Anti-microbial, Anti-inflammatory.

Properties:

- Appearance: Yellow to brown
- Boiling point: (>200°C)
- Specific gravity: 0.9111.[5]

ii. Castor oil:

Biological name: *Ricinus communis*

Chemical constituent: Triglycerides such as 80% Ricinoleic acid, Isoricinoleic acid, Linoleic acid, Stearic acid and Isostearic acid.

Category: Anti-aging and anti-microbial

Properties:

- Appearance: Pale-Yellow or almost colourless
- Boiling point: 313°C
- Specific gravity: 0.95. [6]

MATERIAL AND METHODS

Sodium alginate and calcium chloride were bought from Austria, while propylene glycol and glycerine were obtained via Sisco Research Laboratories in Mumbai. Merck Specialties in Mumbai, India is the source of zinc oxide. Qualigens Fine Chemicals in Mumbai, India is the source of Micro Crystalline Cellulose. Beeswax (White coloured) from Nice Chemicals, Cochin, India. Sodium Benzoate from Mumbai, India's Fine-Chem. Limited. Olive Oil from India's Consumer Manufacture Pvt Ltd. Water that was purified in a laboratory and neem and castor oils that were collected from Natures Naturals India Oils Pvt Ltd, India.

SYNTHESIS OF MICROENCAPSULES

Neem/ Castor oil filled microcapsule were synthesized by ionic gelation method. [7, 8]. Sodium Alginate used as Shell forming agent and Calcium Chloride used as Crosslinker. (Refer the table no.1)

Organic Phase - 1gm Sodium alginate dissolve in 50ml water, under continuous stirring at 1700 rpm 4ml oil neem and castor were added to above solution. The stirring was continued for 10 minutes.

Aqueous (water) Phase -Under continuous stirring at 1700 rpm, 15 g of calcium chloride was dispersed in 100 ml of water aqueous solution. The Organic Phase was then progressively added to the aqueous phase using a 2ml syringe while stirring continuously at 1700 rpm for 20 minutes. After washing two to three rounds of distilled water, the resultant microcapsules were passed through Whatman No. 41 filtering paper and dried at room temperature. [9, 10] (See fig. 1)

CHARACTERIZATION OF MICROENCAPSULE

Analysis of particle size: A particle size analyzer (laser) is used to measure particle sizes. Microcapsule: - Expected particle size: 1-1000 µm. [11]

Infra-red spectroscopy: The functional group that is present in oils and microcapsules containing oils is determined using Fourier transform infrared spectroscopy or FTIR. [12]

Scanning electron microscopy (SEM): The morphology of microcapsules is analysed using a scanning electron microscope. Expected outcome: spherical shape with consistent dimensions. [12]

Thermal gravimetric analysis: Thermal gravimetric analysis (TGA) is a technique that determines a sample's mass over time as temperature varies. Also used to test the stability of microcapsules and essential oils [12].

% Loading efficiency: The essential oil's loading efficiency was assessed using the TGA method. Formula: $LE (\%) = W_{EO} / W_{capsule} \times 100\%$

W_{EO} and $W_{capsule}$ stands for weight loss with essential oils and the initial weight of the capsules as determined by thermal gravimetric analysis, respectively. [13]

Essential oil release test: A dried microcapsule is added to an alcoholic aqueous medium (1:1 volume ratio) to assess the release kinetic. The Essential Oil is evaluate using Ultraviolet-Visible spectroscopy. Data obtained is fitted with the Korsmeyer-Peppas model Equation $-Mt / M_{\infty} = K.t^n$

The few parts of EO released at time t is denoted by M_t / M_{∞} , the release exponent is n, and the release rate constant is k. [13]

FORMULATION OF HERBAL ANTI-AGING CREAM

Herbal antiaging cream is synthesized in batch F₁, F₂, F₃, F₄, F₅. Out of them F₅ batch is observes as most stable having neem and castor oil microcapsules as base and other natural ingredients.

(Refer the table no. 2)

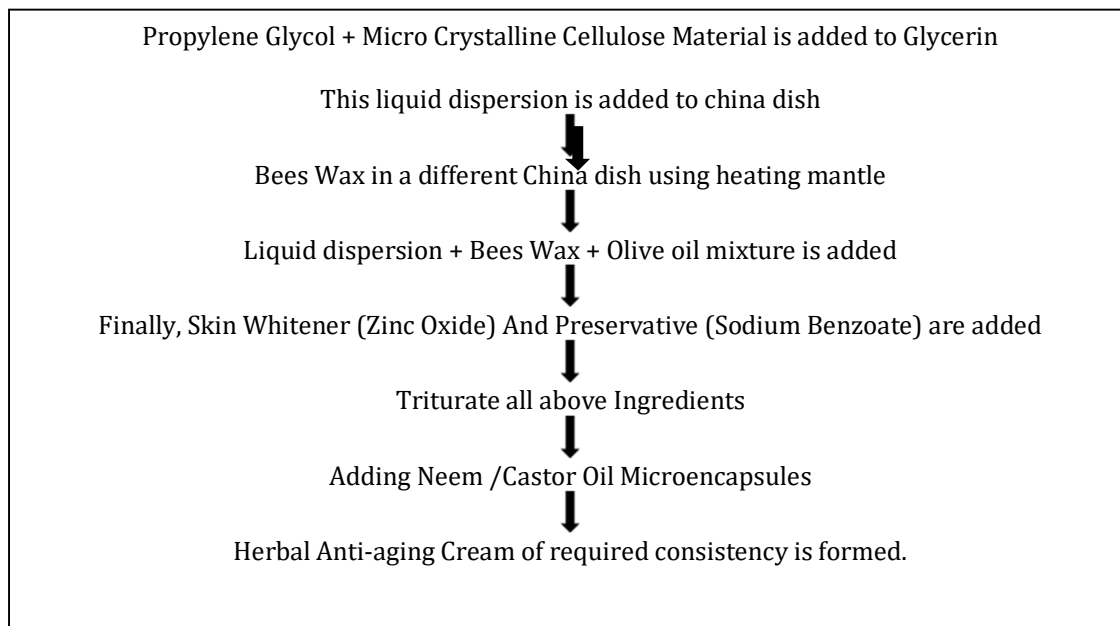


Fig1: PREPARATION OF HERBAL BASED ANTI-AGING CREAM

RESULTS AND DISCUSSION

Synthesis of Microencapsules:

Microcapsules are synthesized using method shown in fig.1 using optimization of trial batches. Neem oil and Castor oil microencapsules are shown in figs. 2 and 3.

Characterization of Microcapsule Scanning Electron Microscopy (SEM)

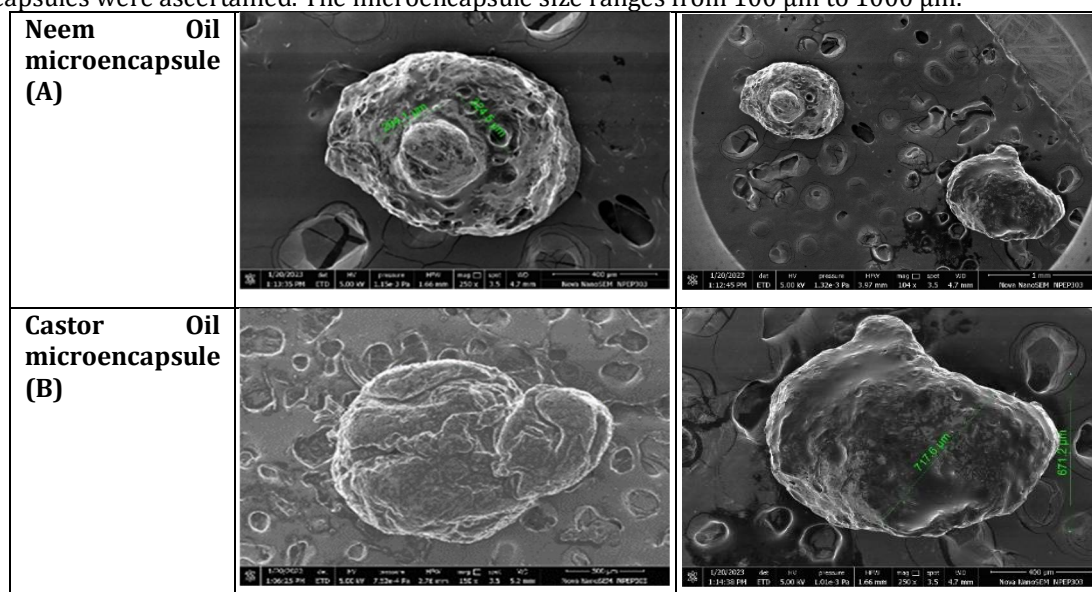
FTIR Spectral Analysis

Thermogravimetric Analysis (TGA)

Loading efficiency (LE)

Scanning electron microscopy (SEM):

A scanning electron microscope (Nova Nano SEM - NPEP 303,5kv) was used to analyze the morphology of the castor oil and neem microencapsules. The samples had already undergone sputtering to coat them with gold. Using image J software, the resulting photomicrographs were processed and the diameters of the capsules were ascertained. The microcapsule size ranges from 100 μm to 1000 μm .



FTIR Spetral Analysis:

FTIR of neem oil and their microencapsules and castor oil and their microencapsules are shown in figs. 4a, 4b, 4c, 4d respectively, refer to table no.3 for functional group identification for same by FTIR.

Thermogravimetric Analysis: TA Instruments' SDT 650 simultaneous thermal analyzer was used to carry out the thermogravimetric analysis. An alumina cup holding an average mass of 10 mg of the substance being tested (Microencapsule) underwent heating at 600 °C at a rate of 100 °C per minute while a nitrogen flow of 50 cm³ min⁻¹ was maintained. To understand the thermal properties of samples, the standard thermogram shows the temperature of maximum degradation (T_{max}) and the starting temperature of deterioration (Tonset) (see figs. 5 A) and 5 B)) Refer to table no. 4 for thermogravimetric analysis of neem oil and castor oil.

Loading efficiency (LE):

Formula:

$$LE (\%) = W_{EO} / W_{Capsule} \times 100\%$$

Where W_{capsule} and W_{EO} refers to the initial capsule weight and essential oil weight loss, determined by TGA, respectively.

a. Neem oil microencapsules:

Initial weight of microencapsule:10mg

Final residue weight: 2.5mg

Essential oil weight loss: Initial weight of microencapsules-Final weight of microencapsule
= 10-2.5
= 7.5mg

$$LE = LE (\%) = W_{EO} / W_{capsule} \times 100\% \\ = 7.5/10 \times 100\%$$

Loading Efficiency = 75%

b. Castor oil microencapsule:

Initial weight of microencapsule:10mg

Final residue weight: 2.8 mg

Essential oil weight loss: Initial weight of microencapsules-Final weight of microencapsule
= 10-2.8
= 7.2mg

$$LE = LE (\%) = W_{EO} / W_{capsule} \times 100\% \\ = 7.2/10 \times 100\%$$

Loading Efficiency = 72%

PHYSICOCHEMICAL EVALUATION OF CREAM FORMULATION

Appearance: The organoleptic characteristics of the cream did not alter after the formulation was stored for an extended period of time. Cream is characterized as Semisolid state, whitish in color, characteristic smell and smooth consistency.

pH of the Cream: Three sample measurements were averaged to get the pH values. It is discovered that the serum's levels fall between 5.85 and 6.87. As a result, every composition was within the skin's typical pH range. pH of cream in F₁, F₂, F₃, F₄ and F₅ Batch is found to be 5.8, 6.0, 6.1, 6.5, 6.7 respectively.

Viscosity: The cream's viscosity, which ranged from 500 to 1000 cps, shows that it can be readily spread with little shear. The spreadability of F₄ and F₅ is better than that of the other formulations. The viscosity of cream for F₁, F₂, F₃, F₄ and F₅ Batch is 5460, 4800, 2499, 3655, 3400.

Spreadability Studies: Spreadability tests conducted on the formulation revealed that the cream spreads more quickly. Spreadability for batch F₁ and F₃ is 13.63 gcm/sec in 11 sec., F₂ and F₅ batch is 15 gcm/sec in 10 sec. and F₅ batch is 18.73 gcm/sec in 8 sec. respectively.

In vitro drug release study:

Refer to Table no. 5 and Fig. 6 for *in vitro* drug release using Neem oil and Castor oil.

Homogeneity: Every formulation results in an even distribution of extracts throughout the cream. Both touch and visual appearance supported this.

In vitro anti-oxidant study:

2,2- diphenylpicrylhydrazyl (DPPH) free radical scavenging assay:

The anti-aging cream that was developed was used in an invitro antioxidant investigation. Table no.6 displays the findings of an *in vitro* model evaluation of the antioxidant activity of ascorbic acid as a standard and at different concentrations of the samples. By scavenging Diphenylpicrylhydrazyl (a free radical) and turning it into Diphenylpicrylhydrazine (a non-radical), the sample demonstrated significant antioxidant activity. The observed radical-scavenging activity was dose dependent. (See fig. 7) Ascorbic acid's scavenging activity surpassed all five of the cream samples collectively. F₅ sample had the highest level of antioxidant activity out of all of them.

Stability Study: The produced Cream formulations were found to be stable after three months of storage; no alterations were noted in terms of their drug concentration, rheological properties, pH, or physical appearance. Stability of F₁, F₂, F₃, F₄ and F₅ cream formulations after 3 months studied and observes as Whitish in colour and pH is 5.3, 5.5,6.4, 6.5, 6.7 and viscosity is 5460, 4800, 2499, 3655, 3400 respectively.

Anti-Microbial study:







The formulation did not exhibit any microbial growth when tested for microbial growth (See fig. 8). It means our formulation is free from microbial contamination. Therefore, cream formulation is safe to use for skin.

After Feel Cream: Good results were seen for emollience, slipperiness and quantity of residue remaining after applying predetermined amounts of cream.




Removal: Using tap water to cleanse the skin made it simple to remove the F₅ cream that had been applied.

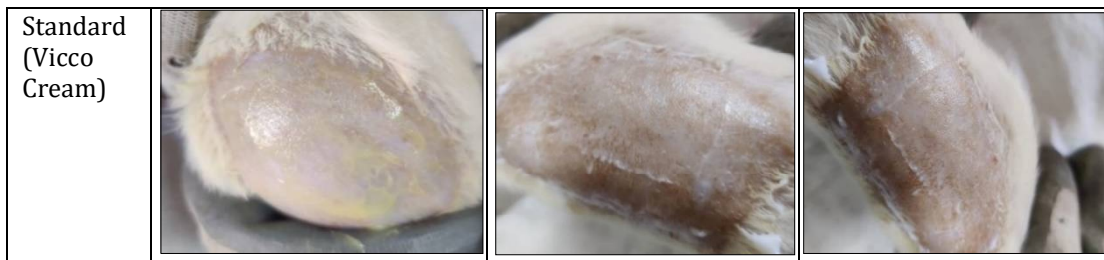
Irritancy Test (Animal Study): Rats' dorsal surfaces were treated with Formulations F₄ and F₅, and after 24 hours, the results were seen. Following application to the skin, formulations F₄ and F₅ exhibit no signs of redness, edema, inflammation, or irritation. It's completely safe to use these formulations on skin.

a. Before Applying Formulation:







	Before Applying Formulation	F ₄ Formulation	F ₅ Formulation
Control			
Standard (Vicco Cream)			

b. After Applying Formulation -

	After Applying Formulation	F ₄ Formulation	F ₅ Formulation
Control			



c. After 24 Hours Observation -

	After 24 Hours Observation	F ₄ Formulation	F ₅ Formulation
Control			
Standard (Vicco Cream)			

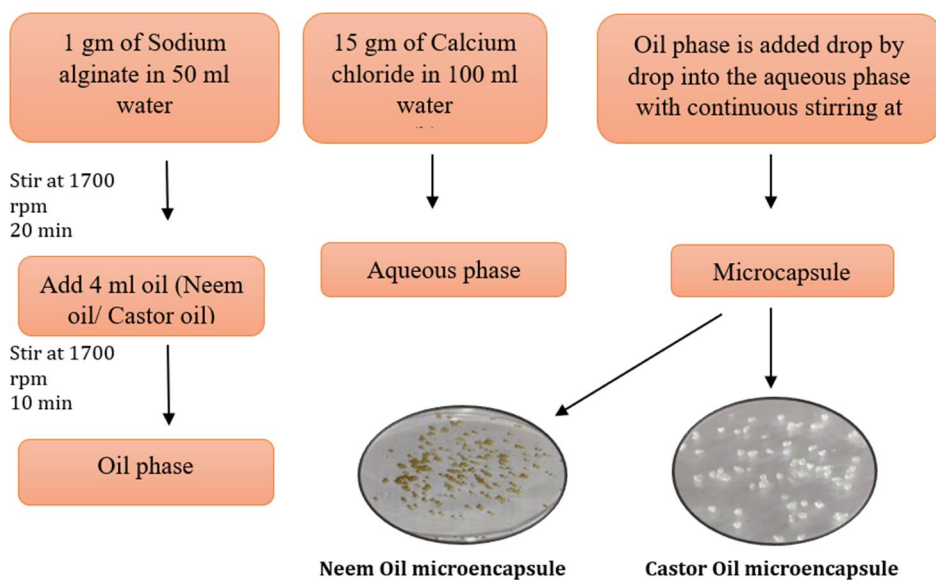


Fig.1 Flow chart for the preparation of the microcapsule containing Neem and Castor Oils

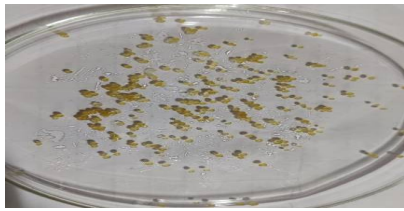


Fig.2 Neem Oil Microencapsules

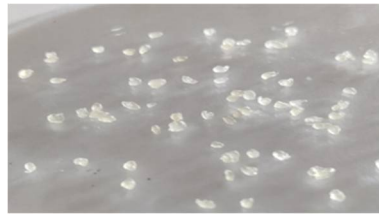


Fig.3 Castor Oil Microencapsules

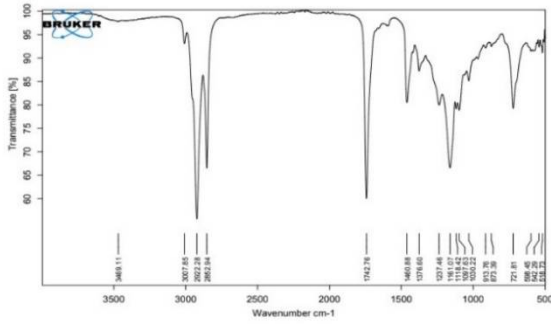


Fig. 4a. Neem Oil

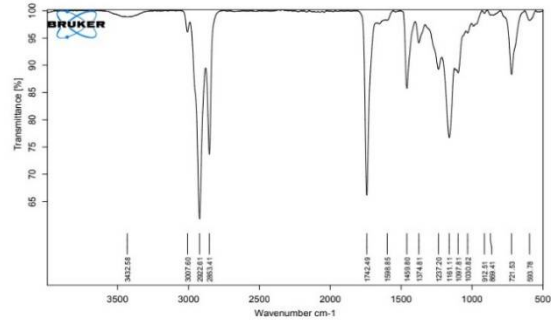


Fig. 4b. Neem Oil microcapsule

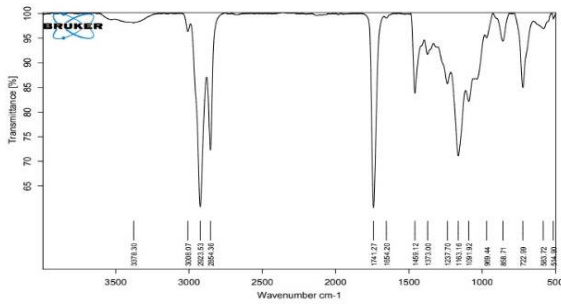


Fig. 4c. Castor Oil

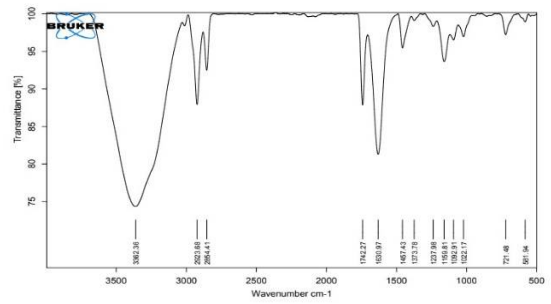


Fig. 4d. Castor Oil microcapsule

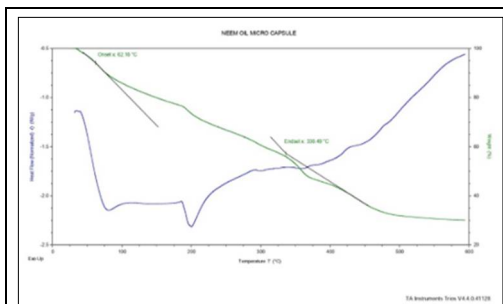


Fig.5 A) Thermogram of Neem Oil Microcapsule

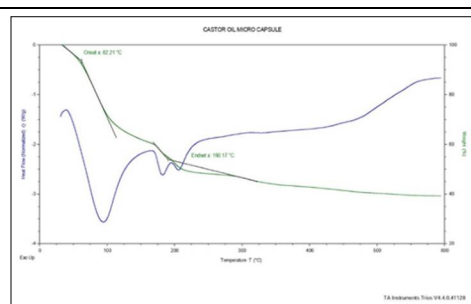


Fig.5 B) Thermogram of Castor Oil Microcapsule

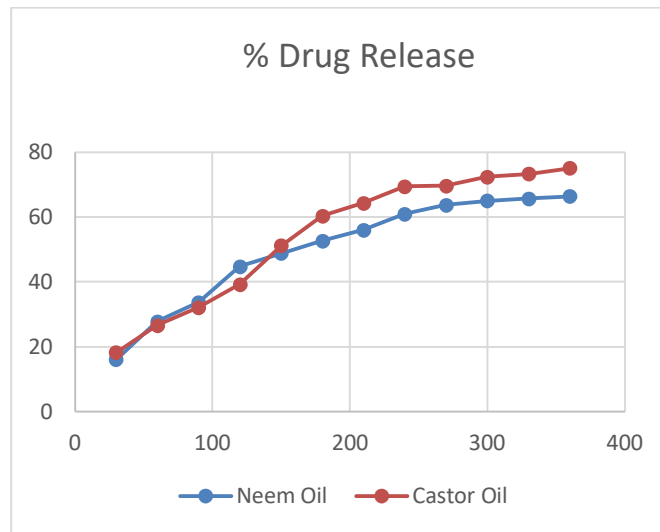


Fig.6 In vitro drug release study

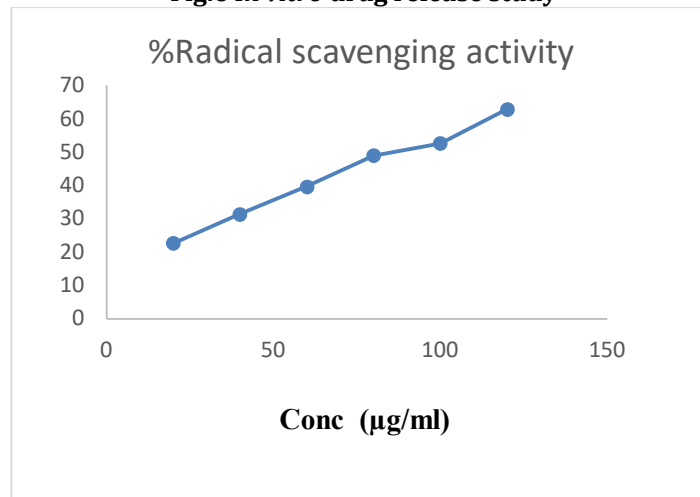


Fig.7 In vitro antioxidant study



Fig.8 Microbial Test

Table No.1 Formulation of Microencapsules

Sr. No	Ingredient	Quantity	Role
1.	Neem oil/ Castor oil	4 ml	Active ingredient
2.	Sodium Alginate	1 gm	Shell forming agent
3.	Calcium Chloride	15 gm	Crosslinker
4.	Deionized Water	150 ml	Aq. Solvent

Table No.2 Formulation of Herbal Anti-aging Cream

Sr. No	Ingredients used	Category	F ₁	F ₂	F ₃	F ₄	F ₅
1.	Neem Oil Microcapsules	A.P.I	0.5 gm	0.5 gm	0.5 gm	0.5 gm	0.5 gm
2.	Castor Oil Microcapsules	A.P.I.	0.5 gm	0.5 gm	0.5 gm	0.5 gm	0.5 gm
3.	Glycerin	Moisturizer	2 ml	2 ml	4 ml	4 ml	4 ml
4.	Propylene Glycol	Humectant	2 ml	2 ml	2 ml	2 ml	4 ml
5.	Zinc Oxide	Skin Whitener	0.5 gm	0.5 gm	1 gm	1 gm	1 gm
6.	Micro Crystalline Cellulose	Stabilizer	-	-	2 gm	2 gm	4 gm
7.	Bees Wax	Emulsifying agent	1 gm	-	2 gm	2 gm	4 gm
8.	Sodium Benzoate	Preservative	1 gm	1 gm	2 gm	2 gm	2 gm
9.	Olive Oil	Vitamin-A Source	2 ml	2 ml	2 ml	4 ml	4 ml
10	Purified Water	Vehicle	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.

Table No.3 Functional group Identified in Neem oil and Castor Oil Microcapsule

Sr. No	Functional Group	Frequency Wave Number / Peak (cm ⁻¹) (For Neem oil)	Frequency Wave Number / Peak (cm ⁻¹) (For Castor oil)
1	OH Stretch	3469.11	3362.36
2	C-H ₂ Stretch	2922.28	2923.68
3	C-H ₂ Stretch	2852.94	2854.41
4	C=O Stretch	1742.76	1742.27
5	C-H Bend	1460.88	1630.97
6	C-O-C	1161.07	1457.43
7	CH ₃ Bend	721.81	1159.41
8	HC=CH Bend	-	721.48

Table No.4 TGA of Neem and Castor Oil Microcapsule

Sample	T _{onset} (°C)	T _{max} (°C)
Neem oil microcapsule	62	336
Castor oil microcapsule	62.21	190

Table No.5 In vitro drug release study

Time (min)	Neem Oil	Castor Oil
30	16.03	18.22
60	27.81	26.61
90	33.65	32.07
120	44.78	39.21
150	48.78	51.16
180	52.65	60.39
210	56.05	64.28
240	60.97	69.42
270	63.72	69.63
300	65.03	72.35
330	65.69	73.3
360	66.34	75.08

Table No.6 Antiaging cream's DPPH scavenging assay with the conventional ascorbic acid

Conc. (µg/ml)	Control absorbance (Ascorbic acid)	Sample absorbance	% Radical Scavenging Activity
20	0.53	0.41	22.64
40	0.51	0.35	31.3
60	0.48	0.29	39.58
80	0.43	0.22	48.83
100	0.4	0.19	52.5
120	0.35	0.13	62.85

CONCLUSION

In above research work we have synthesised neem oil microencapsule and castor oil microencapsule by using ionic gelation method. These microencapsules was characterized by using SEM, TGA, LE and FTIR. The synthesised microencapsules having spherical shape with smooth, rough outer surface having size ranging from 100- 1000 µm which was determined by SEM. The chemical composition of manufactured microencapsules and component neem oil and castor oil has been determined by the primary molecules present in the microcapsule by FTIR spectroscopy. These castor and neem oil microencapsules are incorporated into an herbal cream formulation. Stability experiment results indicated that there was barely any modification in the chemical and physical characteristics. Because the F₅ cream contains a lot of natural ingredients, its microencapsulated base and composition are safer and more stable for up to three months, producing a synergistic impact without any undesirable side effects. Batch F₅ shows good antioxidant property as compare to other formulated batches which was confirmed by performing *In vitro* antioxidant study (DPPH assay). Since oxidative stress is directly related to wrinkling and aging of skin and formulated herbal cream reduces the oxidative stress, therefore formulated herbal cream shows good anti-wrinkling and anti-aging effect.

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CONFLICT OF INTEREST

The Author has no conflict of interest.

REFERENCES

1. Bosset, S., Barré, P., Chalon, A., Kurfurst, R., Bonté, F., André, P., ... & Nicolas, J. F. (2002). Skin ageing: clinical and histopathologic study of permanent and reducible wrinkles. *European Journal of Dermatology*, 12(3), 247-52.
2. Khole, O. A., & Bahiram, K. (2023). Formulation and Evaluation of Anti aging Cream. *International Journal of Pharmaceutical Sciences*, 1(05), 1-1.
3. Luchowska, A., Sroczyńska, M., & Żaczek, A. (2023). Acne medication as a potential solution for slowing down the aging process—a systematic review. *Journal of Education, Health and Sport*, 13(2), 172-176.
4. Antal, D. S., Avram, Ş., & Heinrich, M. (2023). Skin: benefits of natural products in topical applications. *Frontiers in Pharmacology*, 14, 1305705.
5. Bagle, A. V., Jadhav, R. S., Gite, V. V., Hundiwal, D. G., & Mahulikar, P. P. (2013). Controlled release study of phenol formaldehyde microcapsules containing neem oil as an insecticide. *International Journal of Polymeric Materials and Polymeric Biomaterials*, 62(8), 421-425.
6. Patel, V. R., Dumancas, G. G., Viswanath, L. C. K., Maples, R., & Subong, B. J. J. (2016). Castor oil: properties, uses, and optimization of processing parameters in commercial production. *Lipid insights*, 9, LPI-S40233.
7. Xiao, Z., Xu, Z., & Zhu, G. (2017). Production and characterization of nanocapsules encapsulated linalool by ionic gelation method using chitosan as wall material. *Food Science and Technology*, 37, 613-619.
8. Tan, L. H., Chan, L. W., & Heng*, P. W. S. (2009). Alginate/starch composites as wall material to achieve microencapsulation with high oil loading. *Journal of Microencapsulation*, 26(3), 263-271.
9. Sagiri, S. S., Anis, A., & Pal, K. (2016). Review on encapsulation of vegetable oils: strategies, preparation methods, and applications. *Polymer-plastics technology and engineering*, 55(3), 291-311.
10. Jamekhorshid, A., Sadrameli, S. M., & Farid, M. (2014). A review of microencapsulation methods of phase change materials (PCMs) as a thermal energy storage (TES) medium. *Renewable and Sustainable Energy Reviews*, 31, 531-542.
11. Patil, D. K., Agrawal, D. S., Mahire, R. R., & More, D. H. (2016). Synthesis, characterization and controlled release studies of ethyl cellulose microcapsules incorporating essential oil using an emulsion solvent evaporation method. *American Journal of Essential Oils and Natural Products*, 4(1), 23-31.
12. Kim, I. H., Seo, J. B., & Kim, Y. J. (2002). Preparation and characterization of polyurethane microcapsules containing functional oil. *Polymer (Sehur)*, 26.
13. da Silva Barbosa, R. F., Yudice, E. D. C., Mitra, S. K., & dos Santos Rosa, D. (2021). Characterization of Rosewood and Cinnamon Cassia essential oil polymeric capsules: Stability, loading efficiency, release rate and antimicrobial properties. *Food Control*, 121, 107605.
14. Bhaskar, G., Arshia, S., & Priyadarshini, S. R. B. (2009). Formulation and evaluation of topical polyherbal antiacne gels containing *Garcinia mangostana* and *Aloe vera*. *Pharmacognosy magazine*, 5(19), 93.
15. Matangi SP, Mamidi SA, Raghavamma ST, Nadendla RR. Formulation and evaluation of anti aging poly herbal cream. *skin*. 2014;5(6).
16. Yadav, A., Mishra, D. K., Paliwal, P., Farooqui, N., & Gawshinde, A. (2021). Formulation and evaluation of polyherbal antiaging cream. *Asian Journal of Pharmacy and Technology*, 11(4), 284-288.

17. Wu, I. Y., Bala, S., Škalko-Basnet, N., & Di Cagno, M. P. (2019). Interpreting non-linear drug diffusion data: Utilizing Korsmeyer-Peppas model to study drug release from liposomes. *European journal of pharmaceutical sciences*, 138, 105026.
18. Saini R, Mittal A, Rathi V. Formulation & in-vitro antioxidant analysis of anti-ageing cream of Carica papaya fruit extract. *Indian J. Drugs*. 2016;4(1):8-14.
19. Sekar, M., Sivalingam, P., & Mahmad, A. (2017). Formulation and evaluation of novel antiaging cream containing rambutan fruits extract. *International Journal of Pharmaceutical Sciences and Research*, 8(3), 1056.

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