INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

Review Paper

Evalution and Formulation of Alovera and Neem

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ARTICLE INFO

Published: 17 May. 2025
Keywords:
Aloe-vera gel, Fungal infection, Nanoemulgel, Nanoemulsion, Neem oil
DOI:
10.5281/zenodo.15450203

ABSTRACT

India has rich tradition of plant-based knowledge of healthcare. Modern pharmaceutical technology is being combined with traditional health medicines to increase the efficacy. Fungal infection is now the fourth most common infection in the world. For topical delivery, poor permeability of drugs leads to high cost of therapy and decreased patient compliance. This problem can be overcome by preparing lipid based colloidal sub-micron drug delivery. Due to this technology high concentration of drug can be penetrate into the skin as the lipophilic intracellular pathway of skin allows penetration of materials of less than 20nm, hence drug depot is created in the stratum corneum and epidermis. The present study was aimed to formulate herbal nanoemulgel containing neem oil extract and aloe-vera gel for the treatment of f cutaneous fungal infection against the Candida albicans. Nanoemulsion formulations were prepared by spontaneous emulsification method and characterization of the prepared nanoemulsion formulations were done and optimized NE formulation was incorporated into gel base to obtain nanoemulgel. From the results it can be concluded that nanoemulgel formulation is potential and effective topical drug delivery system for neem oil and aloe-vera gel for the topical treatment of fungal infections.

INTRODUCTION

Nowadays, herbal remedies are used for the treatment of various health conditions. The aim of department of AYUSH (Ministry of health) is the growth and development of indian medical systems for the health care delivery. Modern pharmaceutical technology is being combined with traditional health medicines to increase the efficacy. Fungal skin infection has increased in the last two decades. It is now the fourth most common infection in the world. Immobility, mucositis, use of antibiotics, radiation therapy, certain immunosuppressive agents and intensive care units are the various factors responsible for the fungal infections. Candida species are responsible for the variety of the infections ranging from superficial, cutaneous-mucosal to

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Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

deep seated infections. There are various types of candidiasis or yeast infections which is caused by C. albicans out of which reoccurrence rate of cutaneous candidiasis is more and it is rarely cured. In the present study Candida albicans is selected to assess the susceptibility patterns against the phytochemical extracts. For topical delivery, poor permeability of drugs leads to high cost of therapy and decreased patient compliance. This problem can be overcome by preparing lipid based colloidal sub-micron drug delivery. Due to this technology high concentration of drug can be penetrate into the skin as the lipophilic intracellular pathway of skin allows penetration of materials of less than 20nm, hence drug depot is created in the stratum corneum and epidermis. Nano emulsions with uniform distribution of particle size offers several advantages for topical and transdermal delivery of drugs. Reduction in the globule size as compared to conventional gel helps to cross the barrier membrane e (Stratum corneum) of skin which helps in increased efficacy and permeability and reduced treatment time.

Nano emulsions

Nano emulsions are nano-sized emulsions which are manufactured for improving the delivery of active pharmaceutical ingredients. Nano emulsions are thermodynamically stable dispersions of oil and water having a droplet size of less than 100nm stabilized by an interfacial film of surfactant and co-surfactant molecules.

There are 3 types of nano emulsions

1. Oil in water nano emulsions
2. Water in oil nano emulsions
3. Bio-continuous nano emulsion

Formulation techniques of nano emulsions

1. High energy methods
. High-pressure homogenization
. Micro fluidization
. Ultrasonication
. Phase inversion method
. Spontaneous emulsification
. Solvent evaporation
. Hydrogel method

Formulation containing Nanoemulsion in gel base are called nanoemulgel, is the addition of nanoemulsion system integrated into gel matrix which influences a better skin permeation. This mixture of nanoemulgel acts as drug reservoirs, influencing the release of drug from inner phase to outer phase and further. Nnaoemulgel on intact with skin release the oil droplets from the gel and this oil droplets penetrate into the SC of the skin and deliver the drug to intended site. gel have a good adhesion property and high solubilizing of drug in oil phase leads to larger concentration gradient towards the skin that further increase skin penetration of drug. Also, patient compliance is increased due to improved spreadability compare to ointments and creams and decreased stickines

MATERIALS AND METHODS

MATERIALS

Neem seed oil was purchased from NagarjunPharmcauticals Ltd.Gandhinagar, Gujrat. Tween 80, Carbopol934 and PEG 400 was obtained from Loba Chemicals, Mumbai. Aloe-vera gel was purchased from Green Pharmacy, Pune. Triethanolamine is obtained from Qualigens. All the chemicals used were of analytical grade and double distilled water was used throughout the study.

Reformulation Studies

The overall objective of preformulation testing is to generate information useful for the development of formulation.

a) Appearance and colour

The Neem seed oil was examined for its organoleptic properties like colour and appearance

b) Boiling point determination

The boiling point of neem seed oil was determined by open capillary method using boiling point apparatus.

c) Solubility study

Solubility of Neem oil was determined in various surfactants and co-surfactants by using shake-flask method.

d) UV lambda max and calibration curve

Determination of lambda max and calibration curve of neem Oil in dichloromethane- 0.01ml of neem oil was dissolve in 10 ml of the solvent to obtain 1000ppm stock solution A. 1 ml from stock solution is further diluted upto 10ml with dichloromethane to obtain 100ppm stock B. Then standard solution in the range of 20-120ppm were prepared and scanned between 200-400 nm using JASCO UV spectrophotometer to determine the maximum wavelength.

e) Compatibility study Fourier Transforms Infrared Spectroscopy (FT-IR)

The spectrum of neem oil was evaluated for drug quality. FT-IR was also used as a parameter to determine the incompatibility of any drug-polymer.

Preparation of nanoemulsion

Nanoemulsion formulations are prepared by low energy emulsification method. In this method oil phase containing neem oil and Smix are mixed together in conical flask according to the formulae mentioned below. Then to this mixture water phase is added dropwise, and the above mixture containing both the phases is homogenised by using laboratory homogenizer at 3500 rpm for 30 minutes. All the formulated nanoemulsions are kept overnight to check the stability

Preparation of carbopol gel

Carbopol gel was prepared by incorporating 3% w/v of carbopol 934 in distilled water. Weighed amount of carbopol was taken and dispersed over in distilled water for 2 hours till all the carbopol is soaked, triethanolamine is added after soaking and homogenized for 2hr at 600rpm. After homogenization carbopol gel was subjected for two cycles of sonication for 15 min to expel out the entrapped air bubbles from the prepared gel. Preparation of nanoemulgel Nanoemulgels are prepared by spontaneous emulsification method. Optimised nanoemulsions are incorporated into the gel base to obtain the nanoemulgels. Neem Oil nanoemulsion was then combined with the aloe-vera gel in different concentrations (shown below in Table V.) for the synergistic effect of aloe-vera gel against the fungal infection.

EVALUATION PARAMETERS

A) Evaluation parameters of nanoemulsions

. Particle size measurement – Particle size of nanoemulsions were measured by scattering light intensity at scattering angle 900. Viscosity of the dispersant is 0.8872 and the count rate is 382.1 kcps.

. Zeta potential measurement- Zeta potential of the formulations was measured at 25 0C temperature. Thermodynamic stability studies

. - The nanoemulsions were subjected to following thermodynamic stability tests. Viscosity determination

. - Brookfield viscometer is used to determine the viscosity of nanoemulsion formulations at 10rpm for 3 minutes with spindle 62. Drug content measurement

. - 0.01 ml of formulation was dissolve in 10 ml of dichloromethane. Make sure to dissolve it completely to obtain the stock solution. 1ml from the stock solution is further diluted with dichloromethane upto 10ml and absorbance was measured spectrophotometrically at 243nm. Drug content was then calculated. pH determination

- pH of the formulations were determined by using digital pH meter. The formulation was taken into the beaker, then pH meter is immersed into the formulation and reading were recorded. Same process was repeated three times with the same formulations and average of three was taken as pH. Similar procedure was used for the determination of pH of all formulations.

In-vitro release through cellophane membrane- The in-vitro permeation studies were done using Franz Diffusion cell with the help of cellophane membrane. Cellophane membrane was clamped between donor compartment and receiver compartment. 150mg of the nanoemulsion formulation was kept evenly in the donor compartment. The receiver compartment was filled with the 60ml of phosphate buffer 7.4. It was stirred continuously at 100rpm using Teflon coated magnetic bead and temperature was maintained at 370 ±0.5 0C throughout the experiment. 2ml of the receiver fluid was withdrawn at each one-hour interval and replace with same amount to maintain sink condition. The samples were analysed for drug content using UV-spectrophotometer at 243nm.

B) Evaluation parameters of gel

. Rheology study of gel

. - Brookfield viscometer was used to determine the viscosity of gel at 10 rpm for 3min with spindle 64. pH determination

. - pH of the gel was determined by using digital pH meter. The formulation was taken into the beaker, then pH meter is immersed into the formulation and reading was recorded. Colour- The colour of the formulations were checked against black and white background.

. Odour- The odour of the gels were checked by mixing a little amount of gel in water and by taking smell of it.

. Consistency- Consistency of the formulations were checked by applying the gel on to the skin.

. Homogeneity- All the formulations were tested for occurrence of any aggregate by visual inspection after the gels have been set in the container.

. Greasiness- Greasiness were checked by applying the formulations on to the skin.

Phase separation- Phase separation was observed by visual inspection.

b) Drug content- 10 gm of each gel formulation were transferred in the volumetric flask containing 20ml of dichloromethane and stirred for 30 minutes. The volume was made up to 100ml and filtered. 1ml from the stock solution is further diluted with dichloromethane upto 10ml, and absorbance was measured spectrophotometrically at 243nm. Drug content was then calculated.

c) pH determination- pH of the gel was determined by using digital pH meter. The formulation was taken into the beaker, then pH meter is immersed into the formulation and reading was recorded. Same process was repeated three times with the same formulation and average of three was taken as pH.

d) Viscosity determination- Brookfield viscometer is used to determine the viscosity of nanoemulsion formulations at 10rpm for 3 minutes with spindle 63.

e) Spreadability-Spreadability is determined by apparatus suggested by Mutimer et al (1956) which is suitably modified in the laboratory and

used for the study. It consists of a wooden block, which is provided by a pulley at one end. By this method, spreadability is measured on the basis of 'Slip' and 'Drag' characteristics of emulgels. A ground glass slide is fixed on this block. An excess of Nanoemulsion Gel (about 2 gm) under study is placed on this ground slide. The Nanoemulsion Gel was sandwiched between this slide and another glass slide having the dimension of fixed ground slide and provided with the hook. A 1 Kg weight was placed on the top of the two slides for 5 minutes to expel air and to provide a uniform film of the Nanoemulsion Gel between the slides. Excess of the Nanoemulsion Gel was scrapped off from the edges. The top plate was subjected to pull of 80 gms. With the help of string attached to the hook and the time (in seconds) required by the top slide to cover a distance of 7.5 cm be noted. A shorter interval indicates better spreadability.

Spreadability was calculated by using the formula.

S = M.L /T
Where,
S = spreadability,
M = Weight tied to upper slide,
L = Length of glass slides
T = Time taken to separate the slides completely from each other.

f) Extrudability-The extrudability test was carried out using hardness tester. A 5 gm of Nanoemulsion Gel was filled into the aluminum collapsible tubes. The plunged is subjected to hold the tube properly. The 1gm/cm2 applied for the 30 sec. Then measured the quantity of Nanoemulsion Gel extruded from the tube repeat procedure for three times.

g) Swelling Index-To determine the swelling index of prepared Nanoemulsion Gel 1 gm of gel was taken on porous aluminum foil and then placed separately in a 50 ml beaker containing 10 ml 0.1 N NaoH. Then samples were removed from beakers at different time intervals and put it on dry place for some time after it reweighed. Swelling index was calculated as follows.

Swelling Index (SW) % = [(Wt – Wo) / Wo] ×100
Where,
(SW) % = Equilibrium percent swelling.
Wt = Weight of swollen emulgel after time t.
Wo = Original weight of emulgel at zero time

RESULT AND DISCUSSION

Preformulation study

- Colour- Neem seed oil was found to be yellowish brown in colour.
- Boiling point- Boiling point of neem seed oil was found to be 226oC.
- Solubility study- Neem oil shows maximum solubility in Tween 80 and PEG 400 hence they were selected as surfactants and co-surfactants for further experiments. Ratio of Smix (5:1) is selected as the optimised ratio for the preparation of nanoemulsion formulations depending on the solubility studies.
- Lambda max and calibration curve – lambda max is obtained at 243nm.

Compatibility study (FT-IR) - FTIR characteristics of Neem Seed Oil are also observed in the spectra of physical mixtures of drug and excipient indicating no modification for interaction between the drug and excipients. This proves that there is no potential incompatibility with the drug and the excipients used in the nanoemulgel formulations.

CONCLUSION

In present research work, nanoemulsion of neem oil was formulated by spontaneous emulsification method and characterized for vesicle size, polydispersity index, zeta potential, drug content

and viscosity. Droplet size of all the formulated nanoemulsions are found to be satisfactory in the nanoemulsion range. Polydispersity index indicates homogeneous population of nanoemulsion droplet in formulation.NE5 formulation showed highest transdermal flux across cellophane membrane. From the characterization study of nanoemulsions NE5 was selected as the optimized formulation whch was formulated into nanoemulgel by using carbopol-934 hydrogel and aloe-vera gel in diffeerent concentrations and antifungal activity is determined by petri-plate method and zone of inhibition was calculated. NEG4 shows maximum zone of inhibition which was then compared with marketed (0.2% ketoconazole cream) for various parameters i.e. viscosity, extrudability and drug content. It was observed that nanoemulgel formulation (37.23 ±0.733µg/cm2 /hr) show two-fold increase in transdermal flux as compared to marketed (161.35 ± 0.52µg/cm2 /hr). From the results it can be concluded that nanoemulgel formulation is potential and effective transdermal drug delivery system for neem oil and aloe-vera gel. indicates homogeneous population of nanoemulsion droplet in formulation. NE5 formulation showed highest transdermal flux across cellophane membrane. From the characterization study of nanoemulsions NE5 was selected as the optimized formulation whch was formulated into nanoemulgel by using carbopol934 hydrogel and aloe-vera gel in diffeerent concentrations and antifungal activity is determined by petri-plate method and zone of inhibition was calculated. NEG4 shows maximum zone of inhibition which was then compared with marketed (0.2% ketoconazole cream) for various parameters i.e. viscosity, extrudability and drug content. It was observed that nanoemulgel formulation (37.23 ±0.733µg/cm2 /hr) show two-fold increase in transdermal flux as compared to marketed (16.35 ± 0.52µg/cm2 /hr). From the results it can be concluded that nanoemulgel formulation is potential and effective transdermal drug delivery system for neem oil and aloe-vera gel. indicates homogeneous population of nanoemulsion droplet in formulation. NE5 formulation showed highest transdermal flux across cellophane membrane. From the characterization study of nanoemulsions NE5 was selected as the optimized formulation which was formulated into nanoemulgel by using carbopol934 hydrogel and aloe-vera gel in diffeerent concentrations and antifungal activity is determined by petri-plate method and zone of inhibition was calculated. NEG4 shows maximum zone of inhibition which was then compared with marketed (0.2% ketoconazole cream) for various parameters i.e. viscosity, extrudability and drug content. It was observed that nanoemulgel formulation (37.23 ±0.733µg/cm2 /hr) show two fold increase in transdermal flux as compared to marketed (161.35 ± 0.52µg/cm2 /hr). From the results it can be concluded that nanoemulgel formulation is potential and effective transdermal drug delivery system for neem oil and aloe-vera gel. Thus, can be concluded that nanoemulgel is a safe, effective and promising formulation for the topical treatment of fungal infections.

REFERENCES

1. KokaSweta S, PancholiMamta, Sharma Vijay, GayakwadDevshree, Darwhekar G. N, Rajpal V. Formulation and Evaluation of Topical Antifungal Herbal Gels Containing Hydroalcoholic Extract of Catharanthusroseus and Aloe vera. International Journal of Pharmacognosy and Phytochemical Research 2019; 11(3): 173-176.
2. Mishra JN, Verma NK. A brief study on CatharanthusRoseus: A Review. International Journal Research in Pharmacy and Pharmaceutical Sciences 2017; 2(2): 20-23.

3. Alternative medicine, https: www.ijpe.org/alternative-medicine.htm.
4. J. Pannu, A. McCaarthy, A. Martin, T. Hamouda, S. Ciotti, A. Foothergill et.al. NB-002, a Novel Nanoemulsion with Broad Antifungal Activity against Dermatophytes, other Filamentous fungi, and Candida albicans. Antimicrobial Agents and Chemotherapy Vol.53, 2009, 34-40.
5. Maha E. Elmataeeshy, Magda S. Sokar, Mohammed Bahey EI-Din, Dalia S. Shaker. Enhanceed transdermal permeability of Terbinafine through novel nanoemulgel formulation; Development, in-vitro and in-vivo characterization. Future Journal of Pharmaceutical Sciences. Vol.4. 2018, 18-28.
6. V. Harshitha, M. VenkataSwamy, D. Prasanna Kumar, K. Sai Rani, A. Trinath. Nanoemulgel: A Process Promising in Drug Delivery System. Research Journal of Pharmaceutical Dosage Forms and Technology. 12(2): 2020.
7. ManjitJaiswal, RupeshDudhe, P.K. Sharma. Nnaoemulsion an advanced mode of drug delivery system. Biotechnology. (2015) 5; 123-127.
8. Ronak P. Patel, Jay R. Joshi. An overview on Nanoemulsion: A Novel Approach. International Journal of Pharmaceutical Sciences and Researc 3(12); 2012, 4640-4650.
9. PadmadeviChellapa, Aref T. Mohamed, Eseldin I. Keleb, Assad Elmahgoubi, Ahmad M. Eid, Yosef S. Issa, Nagib A. Elmarzugi. Nanoemulsion and Nanoemulgel as a Topical Formulation. IOSR Journal of Pharmacy, Vol-5, Issue 10. 2015, 43-47
10. Lieberman, H. A., M.M. Rieger, and G.S. Banker, Pharmaceutical Dosage Forms Disperse Systems, Emulsion and Microemulsion, 2, 2014. P. 335-369.
11. Shaji, K. P., S. Umesha and B. P. Salimah, A. Novel Liquid Oral Formulation for Octacosanol an anticanser drug and its stability study. Indian Joiurnal of Research in Pharmacy and Biotechnology 3(3), 2012 p. 186.
12. Bhasker K. et.al. Lipid Nanoparticles for transdermal delivery of flabiprofen formulation, in-vitro, ex-vivo, and invivo studies. Lipids in Health and Disease, 8(6) 2009.
13. Gurjot Kaur, Bedi PMS and Jasjret K. Narang. Topical Nanoemulgel: A Novel Pathway for investigating Alopecia. Journal of Nanomedicine and Nanotechnology, 2017: 8(6), 1-5.
14. Panwar A. S., Upadhyay N., Bairagi M, Gujar S, Darwhekar GN, Jain DF, Emulgel: A Review. Asian Journal of Pharmacy and Life Science.2011: 1(3):335.
15. Vats S, Saxena C, Easwari TS, Shukla VK, Emulsion Based Gel Technique: Novel Approach for Enhancing Topical Drug Delivery of Hydrophobic Drugs. International Journal for Pharmaceutical Research Scholars. 2014; 3(2): 650- 653.
16. GopinathR.A.S. Naidu, Pharmaceutical Preformulation Studies, International Journal of Pharmaceutical and Biological Activities 2011; 2 (5):1391-1400.
17. HayderKadhimDrais and Ahmed A. Hussein Iraq, Formulation, Characterization and Evaluation of Meloxicam Nanoemulgel to be used topically 2017; 26(1):9-16.
18. SupriyaDubhashi, V. Pranay et.al. Studies on extraction and HPLC Analysis of.

HOW TO CITE: Satyam Kumar*, Abhishek Srivastava, Evalution and Formulation of Alovera and Neem, Int. J. of Pharm. Sci., 2025, Vol 3, Issue 5, 2896-2902. https://doi.org/10.5281/zenodo.15450203