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(REVIEW ARTICLE)

Innovative wound therapy: The role of herbal nano formulations

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Abstract

Wound healing is a complex process, and the management of wounds is a challenge. Herbal remedies have now become essential for the management of wound. Various herbal preparations have been reported to speed up the process of wound healing having anti-microbial activity, antioxidant and anti-inflammatory to improving epithelization, neovascularization, formation of granulation tissue, collagen synthesis, and wound contraction. Many single-herb and multi-plant extract preparations have been reported to accelerate wound healing activity in freshly prepared incisional and excisional experimental wound models. However, skin barrier is not easy to permeate and influenced by many factors like high hydrophobicity, poor stability, poor penetration through skin, poor solubility. These factors can be overcome by formulating in to nanotechnology- based drug delivery system to increase their efficacy in wound healing. Nanomedicine has revolutionized the field of pharmacotherapeutics in recent decades, enabling innovative approaches in the field of medicine. Here, we reviewed plant based Nano carriers for wound treatment; the present review examines the available research into the use of Nano carriers in the wound healing of herbal remedies. It identifies the various Nano formulation approaches that have been developed and successfully used as a means to enhance the potential for wound of natural bioactive, including Nano emulsions, liposomes, phytosomes, microspheres, transferosomes, nanoparticles, nanoemulgels, and nanofibers.

Keywords: Wound healing; Herbal extract; Nano formulations; Nanoparticles; Nano emulsions; Nano emulgels; Nanofibers; Liposomes

1. Introduction

Phytomedicines derived from plants is serving as a crucial source of medicine since ancient times, their usage have been increased due to therapeutic efficacy and low incidence of side effects compare to synthetic pharmaceuticals. In the present time, the general population is increasingly enthusiastic about herbal remedies, however there are certain limitations when it comes to herbal medications, certain risk factors associated with self-medication of herbal drugs and the potential for overdose when there is no established guide lines is also one of the factor, the risk of toxicity and poisoning associated with incorrect plant identification or lack of knowledge about the plants. Also, mention that there is no restriction on use of herbal medicines. In addition to the above , there are issues of the poor or uncertain bioavailability of active phytochemical constituents, poor penetration through skin in topically applied herbal drugs. So, Novel drug delivery system have potential to overcome some limitations mentioned above and the integration of these phytomedicines in to nanotechnology, offers a promising pathway for developing safer and more therapeutic effect. Nano carriers are an emerging trend that has yielded some interesting results in the novel phytochemical delivery systems.

Nanotechnology methods are being explored for their potential advantages over plant based preparations in comparison with conventional preparations of plant constituents, which include enhanced permeability, solubility,

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bioavailability, therapeutic activity, stability, improved distribution with in tissues and sustained delivery . The nanotechnology based herbal nano carriers have aroused great interest in treating, preventing disease conditions including wound healing

Medicinal plant have been incorporated in to nanostructured has one of the promising way to enhance efficacy of the topical formulations. The efficacy of the nanostructured based herbal formulations stimulated the authors to research; formulate the plant based nanomaterials produced through different methods and their therapeutic targets in modulating wound healing process.

In contrast, the current review anlyzes the available research into the use of Nanotechnologies for regulating wound. Many studies suggested that specific plant-based nanomaterials which include nanoparticles, noisome, nanofibers, hydrogels and more recently Nano emulsions, nanoemulgels have been developed and successfully applied topically to speed up the wound healing time in comparison with conventional preparations of plant constituents.

The primary aim of this article is to explore different plant-based Nano formulations designed to enhance wound healing.

2. Methodology

An extensive research has been conducted regarding Nano formulations formulated for treating wounds, through multiple databases(Google Scholar, Science Direct, Springer Link, and PubMed) covering all published journals from 2014 to the most current. Key search items used in this study included plant extract, Nano formulations, nanoparticles, Nano emulsion, nanoemulgel, nisome, nanosponges, wound healing.

We have restricted our review to Nano carriers specially applied to wound treatment, including only original research papers with complete assessments are considered

The search was confined to English-language articles. Two independent authors assessed all identified studies for relevance and inclusion. Following the application of inclusion criteria, experimental research focusing on the impact of her-loaded Nano formulations in wound treatment in animals in to this review. Out of the 150 articles gathered (published between 2014 and 2024), 100 were excluded due to non-relevance or lack of access to the original articles

2.1. Data Extraction

For each study, the extracted data encompassed the title, author(s), journal, year of publication, plant active ingredient, type of Nano formulation, standard used, methods, and the outcomes of the study.

3. Results and discussion

Table 1 A Completed summary of data extracted from the chosen published articles on Nano formulations for wound **treatment**

S.No	Type of formulations	Plant	Method of preparation	Parameters asessed	Animal model	Outcome	Reference
1	Nanoemulsion	*licorice*	Spontaneous emulsification	Droplet size, zeta potential and polydispersity index,biochemical analysis	Excision *in vivo* model in Healthy adult male wistar rats	It was concluded from the study that, the nanoemulsion containing lavender essential oil and licorice extract formulations was successfully formulated by spontaneous emulsification that facilitates wound healing on 0, 4, 8, 12, and 16th days of wood production, which include closure, epithelialization, and TGF-β1, type I, and type III collagen genes up-regulation. Significantly, reduced MDA levels and increased SOD and GPX activities were associated with decreased levels of lipid peroxidation. The findings imply that a nanoemulsion formulation with lavender essential oil and licorice extract may promote wood healing.	Kazemi et al 2020[1]
2	Nanoemulsion	*Garlic and ginger*	Ultrasonic cavitation	Droplet size, zeta potential and polydispersity index,Refractive index (RI) and transmittance (T),Viscosity and density,Stability studies	Excision in vivo model in healthy albino rabbits	This study used an ultrasonic method to create nine neomycin sulfate nano-emulsions utilizing ginger and garlic oils. Nine nano-emulsions with sizes ranging from 145 to 304 nm were tested for stability over three months. The thermodynamic stability investigations using freeze-thaw, centrifuge, and heat-cool cycles confirmed the remarkable	Ibrar M et al 2022[2]

						stability of these nanoemulsions. The nano-emulsions remained stable for three months with no noticeable changes in physical properties or phase separation. The nano-emulsions shown superior antibacterial efficacy against both gram-positive and gram-negative bacterial strains compared to neomycin sulphate, the positive control. Furthermore, NEs enhanced wound healing compared to Neomycin sulphate ointment.	
3	Nanoemulgel	*Artocarpus lakoocha Roxb.*	Spontaneous emulsification	*Organoleptic test* *Homogeneity test* *pH test* *Particle size analysis* *Viscosity test* *Spreadability test* *PDGF BB and* *TGF-β1 expression*	Burn wound in vivo model in rats	All nanoemulgel formulations using mobe leaves ethanol extract fulfill quality standards for assessment. Nanoemulgel can promote wound healing in rats by increasing fibroblast cells, PDGF-BB, and TGF-β1 expressions. The post-hoc Tukey's HSD test yielded a concentration of 7%, which was not substantially different from Bioplacenton®, the positive control. The optimal dose of ethanol extract from mobe leaves to treat burn lesions in rats using nanoemulgel is 7%.	Tanjung SA et al 2022[3]
4	Nanoemulsion	*clove*	Spontanenous emulsification	Thermodynamic stability, self-nanoemulsification efficiency, droplet size, polydispersity index (PI), zeta potential (ZP), viscosity, percentage of transmittance (% T), and surface morphology	Excision wound in vivo model in female albino wistar rats	In conclusion, essential oils such as clove essential oil have multiple uses and can be employed in industrial applications including in the production of pharmaceutical products and in the manufacture of foods and beverages. Essential oils' therapeutic activities have	Parwez Alam et al 2016[4]

						been promoted using new stable lipid-based systems, known as nanoemulsions. In the present investigation, a nanoemulsion of clove essential oil was formulated and evaluated using an experimental rat model. The results demonstrated that the nanoemulsion had better wound healing property than clove essential oil alone and a reference antibiotic. The study revealed that the nanoemulsion formulation of the clove essential oil for healing effects might be promising for oral administration.	
5	Gold nanoparticles	*Woodfordia fruticosa*		Spectroscopic analysis, XRD analysis, Hydrodynamic size (DLS) , zeta potential measurements, Viscosity measurement, Spreadability, Antibiofilm activity	Excision and incision in vivo wound model in albino wistar rats	In this research, It's revealed a prospect of biogenic gold nanoparticles for creation of new effective therapy for chronic wounds and sepsis in comparing with traditional antibacterial agents regarding to heal the wound and prevent bacteria's resistance. This approach may provide a potentially effective means of eradicating antibiotic resistance and bacterial infections while emphasizing the significance of environmentally friendly synthesis.	Raghuwanshi, N et al 2017[5]
6	Solid Lipid Nanoparticles	*Berberis*	Hot high-pressure homogenization	Optical Microscopy, Field Emission Scanning Electron Microscopy (FESEM), Particle Size, Polydispersity Index (PDI), Total Drug Content (TDC), Entrapment Efficiency (EE) Zeta Potential, Fourier	Excision in vivo wound model in male Lacca mice	In this study, wound formation is a process that involves various phases; there is thus need to have an overall approach when treating such wounds so that we can obtain the best results without compromising on the	Sharma, N., et al 2023[6]

				Transform Infrared Spectroscopy (FT–IR),Differential Scanning Calorimetry (DSC), Hot-Stage Microscopy (HSM), Thermogravimetric Analysis (TGA), Powder X-ray Diffraction (PXRD), Rheological Studies, Texture Analysis		health of the patients and the prevalence of bacteria that are resistant to various antibiotics. However, there are some challenges with the current methods of traditional treatment that restrict their applicability in clinical practice. When traditional remedies are incorporated into the modern medicines for wound care, there is need for accurate tools and technology to produce effective, cheap and secure formulations. Nanoparticulate system can enhance the properties of the plant extracts such as Berberis for speedy and efficient wound healing. There is a need to discover innovative drug delivery systems that can augment the efficacy of single herb Berberis that can further the healing process and avoid infections. This can help with enhancing the effectiveness of the treatment and provide a better solution for wound care.	
7	Silver Nanoparticles	I*ndigofera aspalathoides*	Solvent displacement method	UV-visible absorbance spectroscopy analysis, SEM analysis, FTIR spectroscopy analysis, EDAX spectrum measurements, XRD measurement,	Excision model	Indigofera aspalathoides, can be used to prepare green silver nanoparticles through a process that is quite straightforward, and friendly to the environment. Silver nanoparticles are synthesized from plant extract because the extract contains phytochemicals that assist in the reduction of silver ions and subsequent formation of nanoparticles. It is important to	Arunachalam, K.D.,et al 2013[7]

						prove successful synthesis of cobalt ferrite nanoparticles; the nanoparticles were analyzed using UV-visible spectroscopy, SEM, EDAX, FTIR, and XRD techniques. This work further revealed that the formed nanoparticles of silver from Indigofera aspalathoides extract can potentially be used in wound healing treatments in form of hydrogel dressing. As this study reveals, medicinal plants that are sourced naturally might be used in green synthesis of nanoparticles for application in the medical sector.	
8	Nano silver nanohydrogel	*Aloevera and curcumin*	chemical polymerization	Energy dispersive X-ray microanalysis (EDX) Fourier transforms infrared spectroscopy (FTIR) Dynamic light scattering (DLS) High resolution transmission electron microscopy (HRTEM) . Scanning electron microscopy (SEM)	Excision in vivo wound model in male swiss albino mice of Balb/C strain	Therefore, the incorporation of nanosilver hydrogels, Aloe vera gel, and curcumin on polyester fabric has shown appreciable outcome in regenerative and antimicrobial properties. Further, the nanosilver hydrogel dressing was proved to release silver ions continuously and reduce bacterial colonization effectively. The integration of Aloe vera has proved to improve the wound healing property and when used along with curcumin the antimicrobial property was slightly lower. In conclusion, the gel/nSnH/Aloe dressings were seen as having the greatest potential in healing the wound and reducing the formation of scar tissue. More work in this area might produce better wound dressing materials that	Anjum, S.,et al 2016[8]

						are more effective than those currently in the market.	
9	Nanoemulgel	*Eucalyptol*	Solvent emulsification diffusion	Stability Studies Organoleptic Evaluation Viscosity Measurements Determination of Spreadability Drug Content Analysis In Vitro Drug Release Evaluation Determination of pH Zeta Potential and Particle Size Determination FTIR Studies	Excision in vivo wound model in male albino rabbits	This study showed wounds are one of major causes of death globally.topical drug delivery systemare prefereed over the oral drug delivery systems in the treatment of wounds. It f also ocused on developing euca;y[tol loaded nanoemulsgels for wound closure.based on the results obtained optimized the F5 formula was stable, had a desirable PH and possessed proper wound healing properties.when standard group compared with treatement it was evident that wound closure is great with F5 formulated nanoemulsgel and could be effective in wound healing.	Rehman, A.,et al 2022[9]
10	Nanoemulsion	*flavonoid-enriched oil palm*	Sonication	Stability Studies Organoleptic Evaluation Viscosity Measurements Determination of Spreadability Drug Content Analysis Determination of pH Zeta Potential and Particle Size Determination	Excision laser wound creation in zebrafish	As for the OPL-FEE and OPL-FEE-NE, the present study revealed that they both accelerated the wound healing in the adult zebrafish. Of the two forms, the nanoemulsion with particles size of less than 100 nm was more effective than the unencapsulated form. s. The administration of 30-day low-dose treatment with the test material has a very effective result in the complete healing of wounds. To that extent, gene expression studies suggested that the substances aided in inflammation modulation and antioxidant activity in wound	Zain, M.S.C.,et al 2021[10]

						healing. Based on OPL-FEE the opportunity for introducing a new botanical based wound healing remedy is seen following the nanoemulsion systems.	
11	Nanoemulgel	*Lemongrass Oil*	*Box-Behnken study design*	*Droplet size and polydispersity index (PDI)* *. Morphological characterization* *Rheological evaluation of FLGO-G* *Ex-vivo permeation study of FLGO-G* *In vitro antioxidant efficiency assay* *In vitro antibacterial efficiency assay* *Skin irritation studies* *In vitro drug release study of FLGO-G* *Thermodynamic stability studies*	Excision invivo wound model in male albino wistar rats	From the study it was concluded that FLGO-G nanoemulgel has potential wound healing effects when comapred with the negative and control group in rats.this study also showed that FLGO-G may be useful for targeted delivery of active ingredient	Bhavana, V., et al 2023[11]
12	Nanosponges	*Murraya Koenigii*	Quasi- emulsion solvent diffusion	Organoleptic properties: Determination of pH Spreadability and Drug Content Stability study Phytochemical tests performed Infrared spectroscopy Particle size analysis Zeta potential Invitro drug release studies Drug containing nanosponges	Burn *in vivo* model in male/female albino wistar rats	Nanosponges are mesh like structure and due to their small sizea nd porous nature they have a capacity to absorb large amount of liquid.the study revealed that F6 formula has vey defined fine particles. In nanosponges it was noticed that free flowing of murraya koenigii incorporated in that and results also suggested that the F6 formulation has remarkablle burn wound healing effect	Jadhav, P.A.,et al 2019[12]

				Differential scanning Calorimetry			
13	Nanoemulsion	*Achyrocline satureioides*	Spontaneous emulsification	droplet size,zeta potential and polydispersity . Skin Permeation/Retention Determination of MPO Activity Cytokine Determination Determination of TBARS Determination of the Total Protein Content	Excision in vivo wound model in male wistar rats	In this study, it was observed that flavonoid rich nanoemulsion containing A. satureioide extract with the help of hydrogel thickening penetrated into deeper layer of damaged skin more effectively. This led to a decrease in inflammation and oxidative stress and an enhancement in the healing process with promoted formation of new blood vessels. The animals did not gain or lose weight, and did not display any changes in the temperature during the treatment. In conclusion, based on the present formulation studies, it is possible to identify their potential in the modulation of wound healing and tissue regeneration processes.	Balestrin, L.A.,et al 2022[13]
14	Nanoemulsion	*Tamarix aphylla*	Homogenizer	Stability Studies Organoleptic Evaluation Viscosity Measurements Determination of Spreadability Drug Content Analysis Determination of pH Zeta Potential and Particle Size Determination Skin irritation studies	Burn in vivo wound model in albino rabbits	Wound healing studies on nanoemulsion with plant extract like TA have also provided optimistic outcomes. It is evident that the nanoemulsion cream is biocompatible, safe and strongly effective in decreasing the healing time of the acid-burn wounds in comparison with other standard treatment method such as silver sulfadiazine. The integration of plant-derived medicine such as TA in nanotechnology offers a new future in wound healing to	Gul, H.et al 2022[14]

						prevent future infections. These findings make a suggestion that; there is need for further research and investigations to confirm these results as well as establish the optimal benefits of nanoemulsion cream containing TA in wound healing.	
15	Nanoemulgel	*Tea tree oil*	Ultrasonic homogenizer	Stability Studies Organoleptic Evaluation Viscosity Measurements Determination of Spreadability Drug Content Analysis Determination of pH Zeta Potential and Particle Size Determination Skin irritation studies	Excision in vivo model in rats	In this study, a nanoemulsion containing tea tree oil was made and mixed with gel to create a formulation for delivering mupirocin topically. This formulation was tested and found to be effective against MRSA bacteria, with the help of tea tree oil. It also showed good wound healing properties in tests. Further research is needed to study its effects on different bacterial strains. Overall, the combination of mupirocin and tea tree oil in a nanoemulgel shows promise for fighting infections and promoting wound healing. The nanoemulgel is a good option for delivering drugs topically	Bujubarah, M.M.,et al 2023[15]
16	Nanogel	*Mikania micrantha*	Emulsification diffusion	organoleptic, homogeneity, pH, and size of particles, Antibacterial Activity	Excision model in rats	In this study, Nano gel containing Mikania micrantha has shown potential for treating diabetic wounds and promoting faster healing. It has a high percentage of wound healing within a short period of time and also exhibits antibacterial activity against common pathogens. This innovative pharmaceutical technology holds promise for	Sumantri, I.B et al 2021[16]

						improving wound healing outcomes.	
17	Nanoemulsion	*Cuscuta chinensis*	High- energy homogenizer	Stability Studies Organoleptic Evaluation Viscosity Measurements Determination of Spreadability Drug Content Analysis Determination of pH Zeta Potential and Particle Size Determination Skin irritation studies Entrapment efficiency Antioxidant activity determinatation	Excision model in rats	In this study,the ethanol C. chinensis seed extract had higher yield and showed antioxidant and anti-inflammatory properties, while the ethyl acetate C. chinensis seed extract had better metal-property, lipid peroxidation inhibition, and antibacterial activity. The flavonoids found in the extracts played a role in their biological activities. C. chinensis seed extract-loaded nanoemulsions were successfully developed for potential use in wound care. This formulation shows promise as an alternative product for wound healing in clinical studies.	Nitthikan, N.,et al 2024[17]
18	Nanogel	*Andaliman Fruit*	-	Stability Studies Organoleptic Evaluation Viscosity Measurements Determination of Spreadability Drug Content Analysis Determination of pH Zeta Potential and Particle Size Determination Skin irritation test	Burn model in wistar rats	In this study,research has shown that Andaliman fruit ethanol extract can be made into a stable nano gel with a concentration of 20% for healing wounds. This has potential for use in pharmaceuticals and cosmetics for delivering Andaliman extract topically.	Janice, J.,et al 2023[18]
19	Nanoemulsion	*Deverra triradiata Hochs*t	Spontaneous emulsification	Stability Studies Organoleptic Evaluation Viscosity Measurements Determination of Spreadability Drug Content Analysis	Excision model in wistar rats	In the research shown that using nanoemulsion formulation of two Deverra species essential oils can improve wound healing by promoting antioxidants, reducing inflammation, increasing growth factors and	Kamel, R.A.,et al 2022[19]

				Determination of pH Zeta Potential and Particle Size Determination Determination of the Surface Area Biochemical Analyses		hydroxyproline levels, and enhancing re-epithelialization. This collaboration between researchers from different disciplines can lead to better treatments for various skin injuries.	
20	Nanoemulsion	*Naringenin*	*Box-Behnken study design*	Stability Studies Organoleptic Evaluation Viscosity Measurements Determination of Spreadability Drug Content Analysis Determination of pH Zeta Potential, Particle Size Determination	*In Vitro* Cytotoxicity Study *Ex Vivo* Mucoadhesive Strength	This study developed a chitosan-coated nanoemulsion formulation containing naringenin (NAR) for the treatment of chronic wounds. The optimized formulation showed a controlled release of NAR, increased muco adhesive strength, and improved wound healing potential in an animal model. The formulation demonstrated low cytotoxicity and accelerated wound healing, suggesting it as a potential platform for wound healing. Further studies are needed to validate the efficacy and safety of the formulation in clinical settings.	Akrawi, S.H.,et al 2020[20]
21	Nanoemulsion	*Sunflower and Rosehip*	High shear homogenizer	Droplet Size, Polydispersion Index (PDI), and Particle Number Analysis,Stability Studies Organoleptic Evaluation Viscosity Measurements Determination of Spreadability Drug Content Analysis Determination of pH Viability and Cellular Uptake	Ex Vivo Studies in Human Organotypic Skin Explant Wound Model In Vitro Penetration Studies Using Human Skin In Vitro Studies in Cell Culture	vegetable oils were successfully emulsified into stable nanoemulsions using phospholipids extracted from sunflower and soybean. The addition of a synthetic surfactant to the emulsifying system resulted in smaller nanoemulsions with enhanced cellular uptake, skin penetration, and wound-healing potential. Nanoemulsions composed only of natural phospholipids	Pereira Oliveira, C.N.,et al 2023[21]

				In Vitro Penetration Studies *Ex Vivo* Studies		targeted the epidermis layer, while those with a synthetic surfactant penetrated deeper. The study highlights the importance of standardizing nanoparticle concentration for reliable wound healing tests. The findings suggest that nanoemulsions based on vegetable oils and natural phospholipids show promise as potential drug delivery systems for the treatment of skin disorders.	
22	Nanoemulsion	*Opuntia ficus-indica*	Homogenization	Droplet Size, Polydispersion Index (PDI), and Particle Number Analysis,Stability Studies Organoleptic Evaluation Viscosity Measurements Determination of Spreadability Drug Content Analysis Determination of pH Ex Vivo Studies Biochemical Analyses Immunohistochemical Detection of TGF-β and VEFG	Excision model in male wistar rats *Ex vivo* Skin Permeation Studies	In this study,it was found that formulations of self-emulsifying olive seed oil improved the wound healing capacity than conventional methods and the study also revealed that OFI-SNEDDS enhance the rate of wound closure,minimized the inflammation process,and encouraged the formation of collagen so faster than the rate of healing than the ointment used as control.	Koshak, A.E.,et al 2021[22]
23	Nanoemulsion	*Hippophae rhamnoides L.*	spontaneous emulsification method	Droplet Size, Polydispersion Index (PDI), and Particle Number Analysis,Stability Studies Organoleptic Evaluation Viscosity Measurements Determination of Spreadability	Excision and diabetic incision wound- healing models in wistar rats *Ex vivo* skin penetration studies	This study suggested that the fatty acid profile of sea bucthorn seed oil through chromatographic analysis,psuedoternary phase diagrams were developed for preparation of nanoemulsions. A comparatively better wound potential was observed in both in	Kaur, T.et al 2018[23]

				Determination of pH Rheological studies Acute irritation test Biochemical parameters Ex vivo skin penetration studies Transmission electron microscopy,		vivo and ex vivo studies with the optimized NG2 formulations	
24	Nanoemulsions	*Cassia alata L.*	Probe sonication	Droplet Size, Polydispersion Index (PDI), and Particle Number Analysis,Stability Studies Organoleptic Evaluation Viscosity Measurements Determination of Spreadability Drug Content Analysis Determination of pH Viability and Cellular Uptake In Vitro Penetration Studies Ex Vivo Studies *Biological Properties of CA Leaf Extracts*	Cytotoxicity assay, cell proliferation assay, cell migration assay,	This study showed that wound dressing contained CA extract was effective in the wound closure when the nanoparticles of CA used at the medium dose	Sangkaew, S.,et al 2022[24]
25	Nanoemulsion-gel	*Pituranthos tortuosus*	high-mechanicalenergy method	Droplet Size Analysis and Distribution Zeta Potential Thermodynamic Stability of the Optimal NE *Gelification and Characterization of the Optimal Nanoemulsion Gel* pH Measurement Rheology Study	Excision model in rat	This study showed established nanoemulsion gel containing the extracted essential oil from the pituranthos tortuosus in tunisia was effective in the wound healing.it also showed enhanced in rate of wound clousure comapred to commercial creams	Bahloul, B.,et al 2024[25]

26	Nanoemulgel	*Curcumin*	high-energy ultrasonication	particle size, poly dispersity index (PDI), zeta potential, viscosity, *HPLC analysis, Ex-vivo skin deposition*	Determination of nitric oxide (NOx) (µmol/g tissue, Determination of tissue malondialdehyde (MDA) (nmol/g tissue) Determination of the skin content of proline, hydroxyproline (HPro) and glycine (mg/g tissue), Determination of myeloperoxidase, prostaglandin E2 (PGE2) and interleukin 1 beta (IL-1β). Myeloperoxidase (MPO), prostaglandin E2 (PGE2)	Cur-NE was prepared from phenylpropanol by ultrasonication and QbD software, the best result being recorded in Smix. The structure of the fine NE was smooth and it had Cur in it, as REE analysis using SEM and TEM revealed. Skin permeation studies depicted the studies depicted the maximum Cur release. Compared with the effects of clove oil and Cur-S, the wound healing effects of curcumin were comparable to those of fusidic acid. It was also noted that Cur-NE had no toxicity, and there were no inflammatory cells identified in wounds. In conclusion, the optimized Cur-NE exhibited good anti-inflammatory action in rat models.	Ahmad, N.,et al 2019[26]
27	Nanoemulsion	*Pepromia pellucida*	High – energy homogenizer	GC-MS profiling of PE, FTIR, *Organoleptic test, Homogeity test, pH test, Particle size analysis, Viscosity test, Spreadability test,* Antioxidant activity of PE by DPPH scavanging activity	Burn model in wistar rats Cytotoxicity test, Cell viability, Estimation of pro-inflammatory cytokines TNF- IL-1 and IL-6	The study showed the prepared nanoemulsion containing peperomia pellucida shown effective result in wound closure in wistar rats by stimulates the collagen formation and decreases in inflammation	Prananda, A.T.,et al 2024[27]

28	Nanoemulsion	*Tinospora smilacina*	High pressure homogenization	Particle size Polydispersity index	*In –vitro* wound healing by scratch assay	this study created a stable nanoemulsion (NE) by combining extracts from T. smilacina and C. inophyllum. The NE contained bioactive compounds from both plants in a single formulation. Flavonoid compounds were identified in the T. smilacina extract, some of which have been previously studied for their medicinal properties. The NE was optimised using statistical techniques and was found to be stable with a small particle size and low polydispersity index (PDI). The NE showed antioxidant activity, improved cell viability, and enhanced wound healing properties compared to the individual plant extracts. The addition of a plant-based water component improved the overall effectiveness of the NE. This study demonstrates the potential of using NEs for various biomedical applications.	Saki, E.,et al 2023[28]
29	Nanoemulsion	*Amomum compactum*	Ultrasonicator	High- performance liquid chromatography, FTIR Characterization, Particle size, Polydispersity index,	Excision model in wistar rats Antibacterial activity,	The results obtained from the synthesized CES-NE pointed out the possibilities of this new system for wound healing and antimicrobial activity.the formulated nanoemulsion is stable with a small particle size.the use of the nanoemulsion had positive effects on wound closure in wistar rats	Nasution, A.N.,et al 2023[29]

30	Nanofibers	*Peppermint*	Crosslinking	Surface morphology, particle size, polydispersity index, Swelling ratio, water vapor transmission rate, FTIR Analysis, TGA analysis,	Excision model in male wistar rats Antibacterial activity, MTT Assay,	the study prepared hydrophilic polyurethane-based wound dressings containing peppermint extract using electrospinning. The addition of crosslinked extract-gelatin nanoparticles controlled the release of the extract, resulting in fast and effective wound healing. The dressings showed antibacterial properties, controlled release, and high absorbency. They promoted tissue granulation, collagen synthesis, and faster wound closure compared to conventional gauze bandages. The dressings were non-toxic and enhanced cell viability. Overall, the extract-containing wound dressings showed great potential for treating diabetic ulcers and bacterial infections.	Almasian, A.,et al 2021[30]
31	Nanoemulgel	*Crinum Latifolium*	High-pressure homogenizer	Solubility analysis, Particle size distribution, Polydispersity index, Zeta potential, Drug content, Transmission electron microscopy , Determination of PH, Viscosity measurement, Spreadability analysis, Thermodynamic stability	In vitro studies	In this study, the nanoemulgel formation of methanolic extract of crinum latifolium was successfully optimized using phase diagrams and design of experiments. The formulation had a stable nanoemulgel,uniform particle distribution,sustained release effect comapred to plain formulation also showed good PH,viscosity,spreadability fot topical application.overall, the nanoemulgel can be used in the	Ankur, P.A.,et al 2024[31]
32	Nanoemulsion	*Blumea balsamifera Oil*		Particle size distribution, Polydispersity index measurement,	Cytotoxicity assay, Antioxidant activity,	This research created the stable and effective novel nanoemulgel using natural emulsifiers and oil	Du, L.,et al2024[32]

				Drug content, Optical microscope, Transmission electron microscopy, Stability studies, Centrifugal stability, In vitro drug release studies	Excision wound model in SD rats Wound contraction	phase. The NEs had small particle size, improved permeation and antioxidant activity,they also showed effective wound healing effect in rats comapred to traditional treatments.	
33	Nanoparticles	*Pluchea indica L.*	Solvent displacement method	High –performance liquid chromatography, Hydrodynamic diameter, Particle size , Polydispersity index measurement	Antioxidant activity, Cell viability, *In vitro* scratch assay	The phytochemical analysis for P. indica branch ethanol extract revealed the content of phenolic acid, flavonoids, tannins, alkaloids, and terpenes. The chief known bioactive compound was established to be 4,5-O-dicaffeoylquinic acid. The extract and nanoparticles were neither cytotoxic to normal human dermal fibroblasts nor to keratinocytes; however, toxic effects were concentration dependent on epidermal and oral mucosal keratinocytes. At some doses, they also increased skin and oral mucosal cell migration probably via the antioxidant activity of the compounds.	Chiangnoon, R.,et al 2022[33]
34	Silver nanoparticles	*Azadirachta indica*	Solvent displacement method	GC-MS analysis, Antibacterial activity	Excision model in male albino mice	In this study, flavonoids and terpenoids was present in neem leaves and established the formation of silver nanoparticles from neem extract. Based on the information presented,these AI-AgNPs were proved to be safe for use and effective in the treatment of wounds,the study also provides that neem silver nanoparticles have great scope for affordable green solutioms	Chinnasamy, G.,et al 2021[34]

						targeting bacterial infections and wound healing	
35	Zinc nanoparticles	*Ziziphora clinopodioides Lam leaves*	Solvent displacement method	UV-Vis spectroscopy, FTIR studies, XRD,SEM,EDS techniques, Particle size	Excision model in rats Wound contraction, Antibacterial activity, Antifungal activity, Cytotoxicity assay,	In this study, they synthesized green zinc nanoparticles from ziziphora clinopodiodes having antibacterial ,antioxidant, antifungal ,properties wound healing in rats.	Mahdavi, B.,et al 2019[35]
36	Silver nanoparticles	*Lansium domesticum*	Solvent displacement method	UV-Vis spectroscopy, FTIR studies, XRD,SEM,EDS techniques, Particle size	Excision model in SD female rats, Wound contraction	In this research, *in vivo* wound healing tests showed enhanced wound closure time,hydroxyproline content,tensile strength and excellent histocompatibility in group treated with 0.1% w/w AgNPs pluronic gel. This investigation provides us with evidence that AgNPs obtained from LD fruit peel extract may be ideal candidates for future studies exploring their use in pharmaceutical and biomedical applications.	Shankar, S., et al 2015[36]
37	Silver nanoparticles	*Meliaazedarach*	Solvent displacement method	UV-Vis spectroscopy, FTIR studies, XRD,SEM,EDS techniques, Particle size,TEM	*In vitro* scratch assay in human fibroblast cell	In this research, silver nanoparticles from morinda Azerra extract was prepared through bio-reduction process. The results showed MA-AgNPs possessed higher bioactivities than the MA-extract and also demonstrated promising wound healing activity.	Chinnasamy, G.,et al 2019[37]
38	Niosome	*Andrographis paniculata*	Dispersion method	UV-Vis spectroscopy, FTIR studies, XRD,SEM,EDS techniques,	Dermal biopsy punch in SD rats	The excellent antibacterial of MA-AgNPs against both gram negative and gram-positive	Jamaludin, R., et al 2021[38]

				Particle size,TEM		bacteria make them suitable candidates for development of antibiotics against species resistant to conventional antibiotics. HDFa cell scratch assay proved MA-AgNPs have higher potential in wound healing than MA-extract. α-amylase and α-glucosidase inhibition proved that the MA-AgNPs have potential antidiabetic activity and DPPH and ABST assays confirmed increased antioxidant activity of MA-AgNPs com-pared to the MA-extract. Cytotoxic effect of MA-AgNPs onCCL-13 .	
39	Nanoemulsion	*Chamomilla recutita L.*	High shear pressure, Sonication	pH, droplet size, polydispersity index (PDI), zeta potential, viscosity,		This antimicrobial activity is further enhanced by incorporating the extract into a Nano emulsion system enhanced in healing process	Tominc, G.C. et al 2024[39]
40	Nanoemulsion	*Calophyllum inophyllum*	high shear homogeniser	Particle size, polydispersity index analysis, TEM, XRD,	In vitro scratch assay in BSR Cells	cell viability results showed that CSONE is less cytotoxic than CSO on BSR cells at diferent concentrations. Likewise, the in vitro cell monolayer scratch (wound healing) assay revealed that CSONE with a concentration of CSO as low as 0.4% gave 100% of wound closure after 48hrs and was comparable with the FGF. Te increase in wound closure by CSONE was possible due to the nanoemulsion size of the droplets	Saki, E.,et al 2022[40]

41	Silver nanoparticles	*Prosopis juliflora*	Solvent displacement method	Poly dispersity index, Zeta sizer Nano, Morphological characterization by TEM,XRD	Excision model in mice	Nanoparticles showed anti bacterial activity and have potential in wound healing faster than standard group.	Arya,G.,et al2019[41]
42	Silver nanoparticles	*Caulerpa scalpelliformis*	cold suspension method	Poly dispersity index, Zeta sizer Nano, Morphological characterization by TEM,XRD	Excision model in albino male rats	C. scalpelliformis extract mediated synthesis of AgNPs shows significant enhance wound healing	Manikandan, R.,et al 2019[42]
43	Nanoemulsion	*Zataria multifora Boiss.*	Ultra-homogenizer	FTIR spectrometer, Transmission electron microscopy	Excision model in wistar rats	*Zataria multifora Boiss have anti inflammatory ,anti microbial properties which make this plant for wound healing activity*	Osanloo, M.,et al 2024[43]
44	Nanoemulgel	*Anredera cordifolia (Ten.) Steenis*	High shear homogenizer	UV-Vis spectroscopy, FTIR studies, XRD,SEM,EDS techniques, Particle size,	Excision model in diabetic animals	*study indicates that it is more effective using the nanoemulgel with binahong extract for the treatment of diabetic wounds in rats having hyperglycemia when compared to the extract alone. It also enhances the thickness of the skins layers and the number of fibroblast cells required for repair work.*	Yusuf, M.S.,et al 2023[44]
45	Silver nanoparticles	*Scutellaria barbata*	Solvent displacement method	TEM, AFM, FTIR and XRD confirms the synthesized silver nanoparticles	Wound sratch assay in fibroblast cell	*Scutellaria barbata extract having antimicrobial activity possess wound healing activity in fibroblast cells*	Veeraraghavan, V.P.,et al 2021[45]
46	Copper nanoparticles	*Falcaria vulgaris*	Solvent displacement method	XRD, FT-IR, UV, TEM, and FE-SEM analysis	Excision model in male rats	*The nanoparticles were characterized from various perspectives and were seen to possess several properties including low toxicity, free radical scavenging, antifungal, antibacterial, and being pro-angiogenic.*	Mohammad Mahdi Zangeneha., et al 2019[46]

47	Silver nanoparticles	*Tridax procumbens*	Solvent displacement method	UV–vis absorption spectroscopy, and Scanning Electron Microscopy	Artificial by punch biopsy in Pangasius hypophthalmus	*Silver nanoparticles of Tridax procumbens were found to be an effective* *remedial measure for wound healing*	Jayasree Ravindran.,et al 2019[47]
48	Liposomes	*Danggui Buxue*	Dispersion-ultrasonic method	Particle size, PDI, zeta potential,	Excision model in SD rats	*DBLTG was successfully prepared by* *Loading DBE into liposomes and then dispersing them in a thermosensitive gel. DBLTG showed greater therapeutic efficacy, as evidenced by faster wound closure than control group*	Meng-Di Cui,et al.,2017[48]
49	Nanofiber	*Moringa*	Electrospinning	XRD, FT-IR, UV, TEM, and FE-SEM analysis	Skin lesion in wistar rat	*Moringa having antibacterial showed potential for wound and study showed moringa incorporated in to nanofibers increased wound healing*	Fayemi, O.E.,et al 2018[49]
50	Nanofiber	*Centella asiatica*	Electrospinning	XRD, FT-IR, UV, TEM, and FE-SEM analysis	Excision wound model in SD rats	*Adding C. asiatica extract in the electrospun membranes improves the rate of wound healing in rats. It shielded against bacteria, fungi and virus invasion, encouraged cell proliferation and enhanced wound healing. The membranes also improved the levels of collagen and neovascularization in the wound site. They also minimized the sticking to the wound surfaces, swelling or pooling of fluids and consistently imparted the extract on the wound without additional dressing change discomforts to the patient. Moreover, these membranes are quite helpful in the healing of the wound.*	Yao, C.H.,et al 2017[50]

From the above conducted systematic review it is observed that wound healing is a dynamic process that engages multiple cellular and physiologic pathways in the body. It is essential that wounds are single-use, as otherwise there may be a risk of development of an infection later and also to prevent healing from occurring properly. So, now to try and make these natural extracts heal wounds better scientists suggests that nnanotechnology plays a significant role in the field of medicine and drug delivery, mainly due to the major limitations and problems that affected conventional pharmaceutical agents, and older formulations and delivery systems

In the Nano particulate and Nano-encapsulated systems provide a controlled release, as well as a targeted delivery, of the active constituent(s) present in the plant extract. as well as a targeted delivery, of the active constituent(s) present in the plant extract.There are studies supporting that the use of nanoformulations improves wound reepithelialization along with reduced levels oxidative stressing. In a similar context, it also helps in enhances the stability of formulations with these technological advancements.

4. Conclusion

In conclusion, the application of nanotechnology in wound healing based on plant formulations can be considered to be reliable and effective. These nanoformulations have been designed to improve the effectiveness of the active compounds extracted from plants in promoting the healing of wounds. The advantages include slow release, site specific delivery, and enhanced stability of the formulations. To this end, evidence indicated that nanoparticulate and nano-encapsulated systems are effective in enhancing wound reepithelialization and decreasing oxidative stress. In summary, nanotechnology based drug delivery systems hold vast promise of altering dramatically the field of wound healing by eradicating barriers to the smart delivery of drugs as well as newer forms of medicine

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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