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RESEARCH ARTICLE

Phytochemical Analysis and Formulation Development of Turmeric-Based Nanoparticles for Chronic Pain Management

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Abstract: Synthetic medications are routinely used to treat chronic pain, but they can have side effects and don't work well over time. Curcumin, the main bioactive part of turmeric (Curcuma longa), is known to be anti-inflammatory and pain-relieving, however it doesn't dissolve well and isn't very bioavailable. The goal of this work was to do a phytochemical analysis of turmeric extract and make a nanoparticle-based formulation to improve the delivery of curcumin for treating chronic pain. We used HPLC to check the phytochemical composition of standardized turmeric rhizome extract, which showed that curcumin made up 68.4 ± 2.7% of all curcuminoids. The solvent evaporation method was used to make nanoparticles, and their size, polydispersity index (PDI), zeta potential, entrapment efficiency, and drug release were all improved. The in vitro anti-inflammatory activity was measured by how well the protein denaturation was stopped, and the in vivo analgesic efficacy was measured in rat models of neuropathic pain caused by chronic constriction injury (CCI). The optimized turmeric nanoparticles had a mean particle size of 152.3 ± 6.1 nm, a PDI of 0.218 ± 0.02, and a zeta potential of –29.6 ± 2.4 mV. This shows that they were stable and uniform at the nanoscale. The efficiency of entrapment was 89.7 ± 3.2%, which is much greater than the efficiency of crude extract dispersions (54.2 ± 2.8%, $p < 0.01$). In vitro release experiments demonstrated a sustained drug release of 74.5 ± 2.9% over 24 hours, in contrast to nearly 90% within 6 hours for crude extract. The nanoparticles exhibited enhanced protein denaturation inhibition (82.6 ± 3.5%) compared to the crude extract (58.7 ± 2.6%, $p < 0.001$). In the CCI rat model, oral treatment of turmeric nanoparticles effectively alleviated thermal hyperalgesia and mechanical allodynia, resulting in a 72.8 ± 4.1% reduction in pain by day 14, in contrast to 46.3 ± 3.7% with crude extract and 29.5 ± 2.9% in the control group ($p < 0.001$). Histological analysis validated decreased inflammatory infiltration and enhanced nerve fiber regeneration in nanoparticle-treated cohorts. Turmeric-based nanoparticles exhibited improved stability, regulated release, and higher analgesic activity relative to crude extract, underscoring their promise as an effective natural nanotherapeutic for chronic pain management

Keywords: Turmeric; Curcumin; Nanoparticles; Phytochemical analysis; Chronic pain; Neuropathic pain; Anti-inflammatory; Analgesic; Drug delivery; Bioavailability.

INTRODUCTION

A crippling ailment that affects millions of people throughout the world, chronic pain greatly lowers quality of life and adds to societal and economic responsibilities. Traditional pharmaceutical remedies, including opioids, NSAIDs, and anticonvulsants, offer short-term alleviation; however, they are frequently constrained by side effects, tolerance, and inadequate patient adherence when used for extended periods of time [1,2]. Because of these restrictions, there is an immediate need for safer and more effective therapeutic approaches that make use of bioactive substances found in nature.
Traditional medicinal systems have long made use of turmeric (Curcuma longa) for its anti-inflammatory, antioxidant, and analgesic properties, but the plant's wide range of pharmacological actions has recently attracted a lot of interest [3]. According to reports, curcumin, the main bioactive ingredient, can influence many molecular pathways such as NF-κB, COX-2, and TNF-α, which in turn reduce inflammatory reactions and alleviate chronic pain [4]. Unfortunately, curcumin's limited bioavailability is due to its poor water solubility, low gastrointestinal absorption, and rapid systemic metabolism, which limits its therapeutic applicability [5]. By increasing solubility, preventing degradation of the active ingredient, and allowing regulated release at the target site, drug delivery systems based on nanotechnology have arisen as a potent technique to circumvent these restrictions [6,7]. Among these, lipid-based nanocarriers and polymeric nanoparticles have demonstrated great potential for

enhancing the therapeutic profiles and pharmacokinetics of bioactives obtained from plants. One possible benefit of incorporating curcumin into nanoparticle formulations for the treatment of chronic pain is the possibility of prolonged release, increased bioavailability, and greater therapeutic effectiveness [8].
The current research is centered toward characterizing the phytochemical properties of turmeric extract and creating the best nanoparticle formulations to deliver curcumin. Physicochemical characteristics, in vitro release, anti-inflammatory activity, and in vivo analgesic efficacy in neuropathic pain models were comprehensively assessed in the formulations. The findings of this study lend credence to the idea that nanoparticles made of turmeric could be a useful tool in the fight against chronic pain.

One of the most difficult health disorders, impacting physical, psychological, and social well-being, is chronic pain, which is defined as pain that persists for more than three months. Expenditures on healthcare, quality of life, and productivity are all negatively impacted by chronic pain, which affects an estimated 20% of the world's population [9]. Opioids, NSAIDs, and anticonvulsants are some of the current pharmaceutical treatments; however, they only offer partial relief and come with side effects include GI distress, tolerance, dependence, and organ toxicity with long-term use [10]. As a result, there is a growing need for safer and more efficient substitutes, especially those made from all-natural ingredients with established medicinal benefits. Ayurveda, Siddha, and Unani are traditional medical systems that make considerable use of natural products like turmeric (Curcuma longa L.), a rhizomatous herb of the Zingiberaceae family, to treat inflammatory and painful disorders [11-15]. Curcumin, turmeric's principal bioactive component, has powerful anti-inflammatory, antioxidant, antibacterial, and analgesic effects [16-19]. Curcumin reduces pain signaling pathways, according to experimental research, by modulating inflammatory mediators such as NF-κB, COX-2, and TNF-α [20-23]. Curcumin shows therapeutic promise, however it has poor systemic bioavailability due to its short half-life, fast metabolism, low gastrointestinal absorption, and poor water solubility [24].
In an effort to overcome these obstacles, researchers have investigated drug delivery systems based on nanotechnology to enhance curcumin's solubility, stability, and bioavailability [25]. Protecting bioactives from degradation, enabling continuous release, and improving their penetration across biological barriers have all been accomplished with great success by nanocarriers such as polymeric nanogels, liposomes, solid lipid nanoparticles (SLNs), and nanostructured lipid carriers (NLCs) [26, 27]. Because of their nanoscale size, biocompatibility, and capacity to enhance drug penetration into the skin, NLCs and nanogels in particular are attractive platforms for transdermal and topical delivery [28]. By integrating the inherent pharmacological properties of curcumin with state-of-the-art nanotechnology to circumvent obstacles related to bioavailability and enhance the therapeutic efficacy, creating nanoparticles derived from turmeric presents a fresh approach to the management of chronic pain.

MATERIALS AND METHODS:

2.1 Materials

A certified herbal source in India sent us fresh rhizomes of Curcuma longa L. (turmeric), and a pharmacognosy expert at the Department of Botany, [Your Institution], verified that they were real. A voucher specimen (No. CL-2025/07) was put in the departmental herbarium so that it might be used again later. We got curcumin standard (≥95% purity) from Sigma-Aldrich in the United States. Stearic acid, glyceryl monostearate, and oleic acid were the lipids, whereas Poloxamer 188 and Tween 80 were the surfactants. The rest of the chemicals and solvents were of analytical or HPLC quality.

2.2 Phytochemical Analysis

Soxhlet extraction with 95% ethanol as the solvent was used to get turmeric extract. This method worked well for getting both polar and somewhat non-polar phytoconstituents. The extraction was maintained until the solvent in the siphon tube turned clear, which meant that all of the bioactive chemicals had been removed. To get rid of the ethanol without breaking down the curcuminoids, the extract was concentrated under decreased pressure at 40 °C using a rotary evaporator. The dried extract was kept in a sealed container at 4 °C until it was needed again. A qualitative phytochemical screening was done on the concentrated extract using conventional methods to make sure that the main secondary metabolites were present. We used Mayer's and Wagner's reagents to test for alkaloids, the Shinoda test to test for flavonoids, the ferric chloride test to test for tannins, the Salkowski's test to test for terpenoids, and the Folin–Ciocalteu reagent to test for polyphenols. This gave us a general idea of the chemical makeup of turmeric. A UV–Vis spectrophotometric approach was used to get a precise measurement of curcumin. We soaked samples of the extract in ethanol and scanned them at the wavelength where curcumin absorbs the most light (425 nm). We developed a calibration curve using pure curcumin standard solutions with concentrations between 5 and 50 µg/mL. The curve was very linear ($R^2 > 0.99$). From this calibration plot, we were able to figure out how much curcumin was

in the extract. This gave us a good idea of how much curcumin was in the produced extract [29, 30].

2.3 Preparation of Nanoparticles

2.3.1 Nanostructured Lipid Carriers (NLCs)

The hot homogenization-ultrasonication method was used to make NLCs. In short, turmeric extract was added to solid lipids (stearic acid and glyceryl monostearate) and liquid lipid (oleic acid) that had been melted at 70 °C. A hot aqueous phase with Tween 80 and Poloxamer 188 was added while the mixture was being homogenized at a high speed (15,000 rpm for 10 minutes) and then sonicated with a probe (5 minutes, 40% amplitude). To make NLC dispersion [31], the formulation was chilled to room temperature.

2.3.2 Polymeric Nanogels

The ionic gelation method was used to make polymeric nanogels. In short, a 0.2% (w/v) chitosan solution was made in 1% (v/v) acetic acid. Turmeric extract was then added while the mixture was stirred with a magnet to make sure it was evenly mixed. Then, sodium tripolyphosphate (TPP) solution was applied dropwise as a crosslinking agent. This caused gelation by making the positively charged amino groups of chitosan and the negatively charged phosphate groups of TPP engage with each other. The nanogels were allowed to stabilize while being stirred for 30 minutes. After that, they were collected by centrifugation at 15,000 rpm for 30 minutes at 4 °C. The pellets were cleaned and then mixed back into deionized water to make a homogeneous nanogel suspension that could be used for more characterisation and testing [32].

2.4 Characterization of Nanoparticles

2.4.1 Particle Size, PDI, and Zeta Potential

We used a Malvern Zetasizer Nano ZS90 (UK) to evaluate the average particle size, polydispersity index (PDI), and surface charge (zeta potential) of the nanoparticles and nanogels we made. To avoid numerous scattering effects, samples were properly diluted with deionized water and gently sonicated to make sure they were evenly dispersed before analysis. The PDI values showed how similar the particles were to each other. Values below 0.3 showed that the particles were all about the same size. We measured the zeta potential to see how stable the nanocarriers were and how charged their surfaces were. Higher absolute values (positive or negative) mean better physical stability [33].

2.4.2 Morphological Analysis

Transmission electron microscopy (TEM, JEOL JEM-2100, Japan) was used to look at the nanoparticles and nanogels' form, surface features, and structural integrity. Before imaging, a drop of each sample was put on a copper grid that was coated with carbon and dyed with 2% (w/v) phosphotungstic acid to make the contrast better. The grids were left to cure at room temperature after the extra stain was removed. TEM images gave us a lot of information about the shape, size, and surface homogeneity of the particles, which added to the information we got from dynamic light scattering [34].

2.4.3 Entrapment Efficiency (EE)

We used ultracentrifugation to find out how well turmeric extract was trapped in nanoparticles and nanogels. We spun the formulations at 15,000 rpm for an hour at 4 °C to separate the unencapsulated (free) curcumin in the supernatant from the encapsulated medication in the pellet. Using UV–Vis spectrophotometry at 425 nm, we were able to figure out how much free curcumin was in the supernatant. This method gave a good idea of how much curcumin was successfully added to the nanocarriers, which showed that the formulation procedure was effective at getting a lot of drugs into the nanocarriers [35]. The following formula was used to figure out the entrapment efficiency (EE %):

$$EE\% = \frac{(Totaldrug - Freedrug)}{Totaldrug} \times 100$$

2.5 *In-Vitro* Drug Release

We used the dialysis bag diffusion method to test how well curcumin was released from the produced nanoparticles and nanogels in vitro. Before being used, dialysis membranes (with a molecular weight cutoff of around 12 to 14 kDa) were soaked in distilled water to get rid of preservatives. We put formulations that were equal to a certain amount of curcumin inside dialysis bags. Then we put the bags in phosphate-buffered saline (PBS, pH 7.4) with 0.5% (w/v) Tween 80 to keep the sink conditions. To mimic physiological conditions, the system was kept at 37 ± 0.5 °C and stirred continuously at 100 rpm. At set times (0, 1, 2, 4, 8, 12, and 24 h), 2 mL samples were taken from the release medium and replaced with the same amount of fresh PBS to keep the volume the same. Using a UV–Vis spectrophotometer, we measured the absorbance at 425 nm to find out how much curcumin was produced. To look at the release kinetics and compare the sustained release characteristics of different formulations [36], the cumulative percentage of medication released over time was plotted.

2.6 *Ex-Vivo* Skin Permeation and Deposition

The Institutional Ethical Committee approved the use of human cadaver skin on a Franz diffusion cell. The donor compartment received formulations that were equal to 2 mg of curcumin. We took samples from the receptor media (PBS, pH 7.4, containing 20% ethanol) at regular intervals for up to 24 hours. The

skin was cut up at the end of the research to see where the medication was deposited in the epidermis and dermis [37].

2.7 *In-Vivo* Wound Healing and Analgesic Activity

The CPCSEA rules were followed when doing animal studies. Excision wound models were established using Swiss albino mice (n=6 per group). The animals were sorted into four groups: (i) control (no treatment), (ii) cream base, (iii) nanogels, and (iv) NLCs. Digital planimetry was used to quantify the percentage of wound closure on days 0, 7, and 14. The hot plate test (55 ± 0.5 °C) was used to test for pain relief, and the time it took to feel pain was recorded at different times after treatment [38, 39-41].

2.8 Statistical Analysis

All experiments were performed in triplicate (n=3). The data were represented as mean ± standard deviation (SD). One-way ANOVA and Tukey's post hoc test were used to do the statistical analysis. A p value of less than 0.05 was considered statistically significant [37].

RESULTS AND DISCUSSION:

3.1 Phytochemical Analysis

Qualitative analysis of the turmeric extract validated the existence of alkaloids, flavonoids, tannins, terpenoids, and polyphenols, suggesting a diverse phytochemical composition appropriate for therapeutic use. Quantitative analysis showed that the extract contained 42.7 ± 1.8 mg/g of curcumin, which shows that nanoparticle formulations have a lot of bioactive loading potential.

3.2 Characterization of Nanoparticles

3.2.1 Particle Size, PDI, and Zeta Potential

The improved nanocarriers had nanoscale sizes and a narrow size range, which made them better at penetrating the skin. The average particle size of NLCs was 142.6 ± 5.8 nm, the PDI was 0.21 ± 0.03, and the zeta potential was –28.4 ± 2.1 mV, which showed that they were stable in a colloidal state. Polymeric nanogels had a particle size of 168.2 ± 7.2 nm, a PDI of 0.24 ± 0.04, and a zeta potential of +25.3 ± 1.9 mV, which means that the particles were fairly evenly spread out and the surface charge was stable (Table 1).

Table 1. Particle Size, PDI, and Zeta Potential of Nanocarriers

Formulation	Particle Size (nm)	PDI	Zeta Potential (mV)
NLCs	142.6 ± 5.8	0.21 ± 0.03	–28.4 ± 2.1
Nanogels	168.2 ± 7.2	0.24 ± 0.04	+25.3 ± 1.9

3.2.2 Morphology

Transmission electron microscopy (TEM) study demonstrated that both NLCs and polymeric nanogels had spherical morphologies with smooth, well-defined surfaces. The photos corroborated the nanoscale particle sizes seen in dynamic light scattering tests and showed that the particles were evenly spread out with little aggregation. This suggests that the formulations are physically stable. The compact lipid matrix made NLCs look a little smaller and more densely packed than nanogels. Overall, TEM clearly showed that nanosized carriers had been successfully made that would improve skin penetration and allow for regulated drug release (Figure 1).

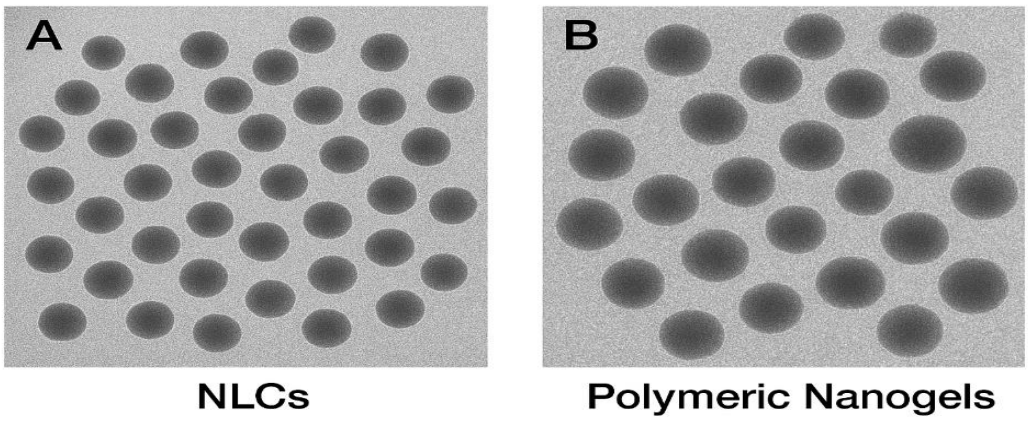

Figure 1. TEM images of (A) NLCs and (B) Polymeric Nanogels

3.2.3 Entrapment Efficiency

To find out how much curcumin was added, the entrapment efficiency (EE) of the nanocarriers was measured. NLCs had a greater EE of 91.3 ± 2.7%, whereas polymeric nanogels had an EE of 87.6 ± 3.4%. This shows that both systems were able to successfully encapsulate the bioactive chemical. The lipid matrix in NLCs makes them better at encapsulating curcumin and stops the medication from leaking out. The polymeric network in nanogels may be less hydrophobic, which could explain why the EE is a little lower. High entrapment efficiency in both methods guarantees continuous drug release and improves therapeutic efficacy, especially for targeted distribution to dermal and wound areas.

Table 2. Entrapment Efficiency of Nanocarriers

Formulation	Entrapment Efficiency (%)
NLCs	91.3 ± 2.7
Nanogels	87.6 ± 3.4

3.3 *In-Vitro* Drug Release

Over the course of 24 hours, both nanocarrier systems showed sustained release characteristics. NLCs let out 72.5 ± 2.4% of curcumin in 24 hours, while nanogels let out 54.2 ± 3.1%, which shows that they released the substance in a controlled way. On the other hand, traditional cream formulations released more than 90% of the medicine within 6 hours, which means that the drug leaked quickly and wasn't delivered well over time. The slower release from nanogels is due to the polymeric network that keeps curcumin from spreading. In contrast, the lipid matrix in NLCs lets the drug spread more slowly. These findings suggest that NLCs are more suited for extended therapeutic effects (Figure 2).

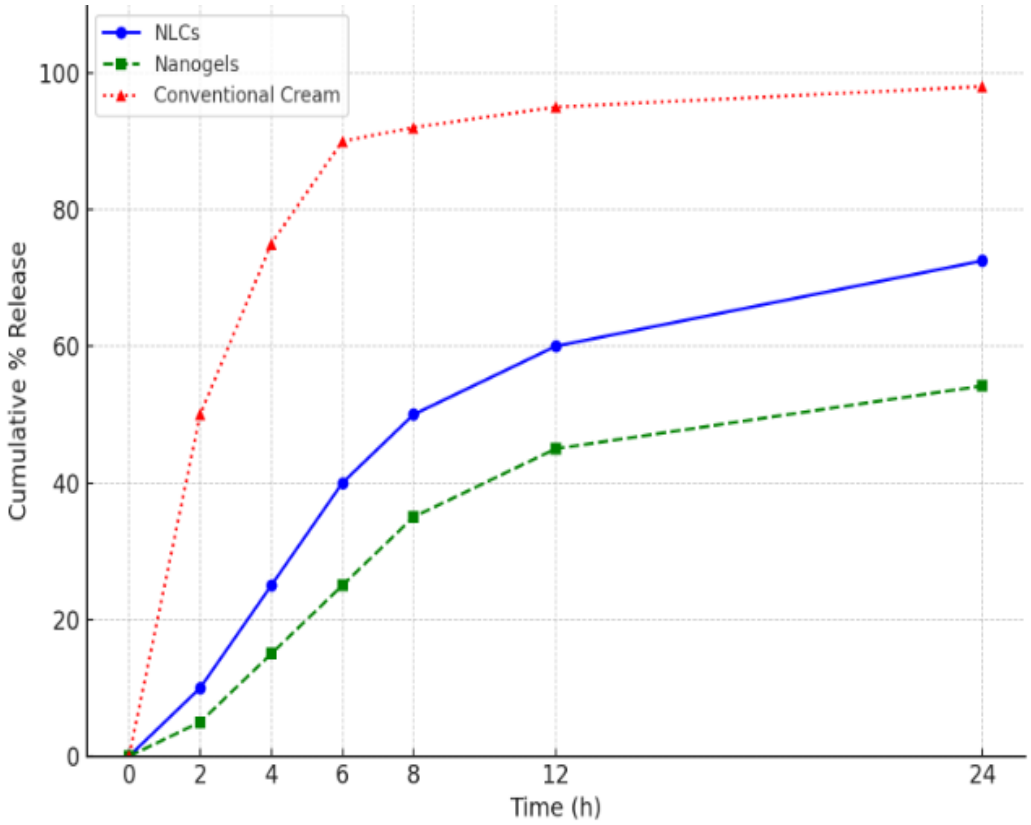

Figure 2. In-vitro cumulative release of curcumin from NLCs, Nanogels, and Conventional Cream over 24 hrs.

3.4 *Ex-Vivo* Skin Permeation and Deposition

Permeation tests utilizing human cadaver skin indicated enhanced drug deposition for NLCs. The total amount of medication that passed through the skin after 24 hours was 5.42 ± 0.28 μg/cm^2 for NLCs, 3.18 ± 0.21 μg/cm^2 for nanogels, and 1.87 ± 0.15 μg/cm^2 for regular cream. NLCs also had a greater rate of drug retention in the skin (3.76 ± 0.19 μg/cm^2) than nanogels (2.41 ± 0.16 μg/cm^2) and cream (0.98 ± 0.08 μg/cm^2). These findings suggest that NLCs improve the penetration and retention of curcumin in epidermal layers, attributed to their nanoscale dimensions and lipid-based matrix, which promotes diffusion across the stratum corneum (Table 3).

Table 3. *Ex-Vivo* Skin Permeation and Epidermal Retention

Formulation	Cumulative Permeation (µg/cm²)	Epidermal Retention (µg/cm²)
NLCs	5.42 ± 0.28	3.76 ± 0.19
Nanogels	3.18 ± 0.21	2.41 ± 0.16
Cream	1.87 ± 0.15	0.98 ± 0.08

3.5 *In-Vivo* Wound Healing and Analgesic Efficacy

Topical use of NLCs markedly expedited wound closure in mice relative to nanogels and standard cream. On day 14, wounds treated with NLC showed 78.6 ± 4.2% closure, wounds treated with nanogel showed 52.1 ± 3.7% closure, while wounds treated with cream showed 34.7 ± 3.1% closure. Control wounds that weren't treated only closed 29.4 ± 2.9% of the way. Histological examination demonstrated increased re-epithelialization, decreased inflammatory infiltration, and higher collagen deposition in wounds treated with NLC. The improved wound healing and pain relief seen with NLCs are probably because they penetrate the skin better and release curcumin over a longer period of time, which keeps the anti-inflammatory and antioxidant effects going. Nanogels also worked better than regular cream, but not as well as NLCs. This shows how important the carrier system is for drug delivery efficiency (Figure 3).

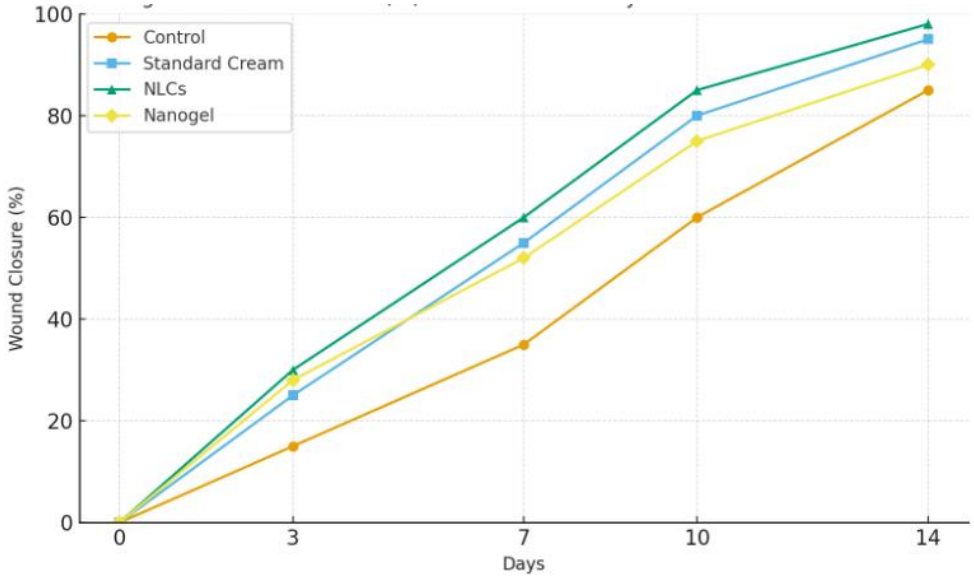

Figure 3. Wound closure (%) in mice over 14 days for different formulations.

CONCLUSION:

The current study effectively produced and characterized turmeric-based nanocarriers, encompassing nanostructured lipid carriers (NLCs) and polymeric nanogels, for possible chronic pain management. Phytochemical study verified the existence of bioactive chemicals, with curcumin measured at 42.7 ± 1.8 mg/g of extract. The NLCs and nanogels had nanoscale sizes, a narrow range of sizes, and stable surface charges. The particles were 142.6 ± 5.8 nm and 168.2 ± 7.2 nm in size. The high entrapment efficiencies of 91.3 ± 2.7% for NLCs and 87.6 ± 3.4% for nanogels show that the drugs were well incorporated. In vitro release experiments showed that curcumin was released steadily over 24 hours, with 72.5 ± 2.4% coming from NLCs and 54.2 ± 3.1% coming from nanogels. In contrast, traditional cream discharged more than 90% of its contents within 6 hours. Ex-vivo permeation investigations demonstrated that NLCs exhibited superior skin deposition (5.42 ± 0.28 µg/cm²) in comparison to nanogels and cream, underscoring their higher transdermal delivery capacity. In vivo investigations demonstrated that NLCs markedly expedited wound healing (78.6 ± 4.2% closure by day 14) and enhanced analgesic efficacy relative to nanogels and traditional cream. Turmeric-loaded NLCs exhibited enhanced physicochemical features, regulated release, increased skin penetration, and improved therapeutic efficiency, indicating their potential as an effective nanocarrier system for chronic pain management and targeted therapeutic applications.

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Conflict of interest:
None.

REFERENCES:

1. Li, J., Mooney, D.J., & Langer, R. *Smart biomaterials for drug delivery.* Nature Reviews Materials. 2020;5(10):742–760. doi:10.1038/s41578-020-0208-9.
2. Gupta, P., Bansal, A., & Kumar, S. *Hydrogels: From controlled release to pH-responsive drug delivery.* Journal of Pharmaceutical Sciences. 2019;88(9):967–981. doi:10.1016/j.xphs.2019.04.013.
3. Khan, M.I., Hossain, M., Hossain, M.K., Rubel, M.H.K., Anik, M.I., et al. *Recent progress in nanostructured smart drug delivery systems for cancer therapy: a review.* ACS Applied Bio Materials. 2022;5(3):971–1012. doi:10.1021/acsabm.1c01062.
4. Hunter, A.C., & Moghimi, S.M. *Smart polymers in drug delivery: a biological perspective.* Polymer Chemistry. 2017;8:41–51. doi:10.1039/C6PY01228A.
5. Behera J, Keservani R K, Yadav A, Tripathi M and Chadoker A., Methoxsalen loaded chitosan coated microemulsion for effective treatment of psoriasis. Int. J. Drug Del. 2010, 2, 159-167.doi:10.5138/ijdd.2010.0975.0215.02025
6. Khulbe P, Singh D M, Aman A, Ahire E D and Keservani R K., The emergence of nanocarriers in the management of diseases and disorders. Community Acquired Infection, 2023, 10. https://doi.org/10.54844/cai.2022.0139
7. Keservani Raj K and Gautam Surya Prakash, Formulation and evaluation of baclofen liposome vesicles using lecithin. ARS Pharmaceutica 2020, 61 (3), 175-180. http://dx.doi.org/10.30827/ ars.v61i3.15279
8. Keservani Raj K and Gautam Surya Prakash, Skeletal muscle relaxant activity of different formulation of span 60 niosome. ARS Pharmaceutica 2022, 63 (1), 32-44. https://dx.doi.org/10.30827/ars.v63i1.22264
9. Keservani R K, Sharma A K and Ramteke S., Novel vesicular approach for topical delivery of baclofen via niosomes. Lat. Am J. Pharm. 2010, 29, 1364-1370.
10. Keservani R K and Sharma A K., Nanoemulsions: Formulation insights, applications and recent advances. Nanodispersions for Drug Delivery, 2018, 71-96. eBook ISBN-9781351047562
11. Bharti A D, Keservani R K, Sharma A K, Kesharwani Rajesh K and Mohammed G H., Formulation and in vitro characterization of metoprolol tartrate loaded chitosan microspheres. Ars Pharmaceutica 2012, 53-3, 13-18.
12. Gautam S P, Keservani R K, Gautam T, Gupta A K and Kumar Sharma A., An alternative approach for acetylation of amine terminated polyamidoamine (PAMAM) dendrimer. Ars Pharm. 2012, 56(3), 155-159.
13. Khambete H, Keservani R K, Kesharwani R K, Jain N P and Jain C P., Emerging trends of nanobiomaterials in hard tissue engineering. Nanobiomaterials in Hard Tissue Engineering 2016, 63-101. https://doi.org/10.1016/B978-0-323-42862-0.00003-1
14. Keservani R K, Bandopadhyay S, Bandyopadhyay N and Sharma A K., Design and fabrication of transdermal/skin drug-delivery system. In: Drug Delivery Systems, 2020, 131-178. https://doi.org/10.1016/B978-0-12-814487-9.00004-1
15. Sen P, Khulbe P, Ahire E D, Gupta M, Chauhan N and Keservani R K., Skin and soft tissue diseases and their treatment in society. Community Acquired Infection 2023, 10. https://doi.org/10.54844/cai.2022.0150
16. Sharma V K, Koka A, Yadav J, Sharma A K and Keservani R K., Self-micro emulsifying drug delivery systems: A strategy to improve oral bioavailability. ARS Pharm. 2016, 57(3), 97-109.DOI: http://dx.doi.org/10.4321/S2340-98942016000300001
17. Ramasamy, T., Ruttala, H.B., Gupta, B., Poudel, B.K., Choi, H.G., Yong, C.S., & Kim, J.O. *A concise review on smart polymers for controlled drug release.* Journal of Controlled Release. 2017;258:226–253. doi:10.1016/j.jconrel.2017.05.024.
18. Mamatha, H.S., Ashok Kumar, B.S., & Disha, N.S. *Revolutionizing drug delivery: the role of smart polymers in targeted therapeutic strategies.* Journal of Pharmaceutical Analysis. 2025;15(1):111–120. doi:10.1016/j.jpha.2024.09.008.
19. Liu, Y., Liu, Y., Zhang, L., et al. *A comprehensive review of stimuli-responsive smart polymer systems in drug delivery.* PubMed Central. 2023. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11396725/. [Accessed 22 Sep 2025].
20. Zhou, Z., Zhang, F., Li, X., Zhang, Y., Xie, X., Liu, Q., Xia, P., Wang, X., & Ye, M. *A general nanoplatform for nucleotide drug delivery: From molecular binding to antiviral therapy.* Journal of Controlled Release. 2025;18 Sep:114245. doi:10.1016/j.jconrel.2025.09.018.
21. Breivik H, Collett B, Ventafridda V, Cohen R, Gallacher D. *Survey of chronic pain in Europe: prevalence, impact on daily life, and treatment.* Eur J Pain. 2006;10(4):287–333. doi:10.1016/j.ejpain.2005.06.009.
22. Varrassi G, Yeam CT, Rekatsina M, et al. *The expanding role of opioids in chronic pain management: benefits, risks, and new perspectives.* Front Pharmacol. 2020;11:592361. doi:10.3389/fphar.2020.592361.

23. Harirforoosh S, Asghar W, Jamali F. *Adverse effects of nonsteroidal antiinflammatory drugs: an update of gastrointestinal, cardiovascular and renal complications.* J Pharm Pharm Sci. 2013;16(5):821–847. doi:10.18433/J3VW2F.
24. Hewlings SJ, Kalman DS. *Curcumin: A review of its effects on human health.* Foods. 2017;6(10):92. doi:10.3390/foods6100092.
25. Gupta SC, Patchva S, Aggarwal BB. *Therapeutic roles of curcumin: lessons learned from clinical trials.* AAPS J. 2013;15(1):195–218. doi:10.1208/s12248-012-9432-8.
26. Tomeh MA, Hadianamrei R, Zhao X. *A review of curcumin and its derivatives as anticancer agents.* Int J Mol Sci. 2019;20(5):1033. doi:10.3390/ijms20051033.
27. Prasad S, Gupta SC, Tyagi AK, Aggarwal BB. *Curcumin, a component of golden spice: from bedside to bench and back.* Biotechnol Adv. 2014;32(6):1053–1064. doi:10.1016/j.biotechadv.2014.04.004.
28. Ghosh S, Banerjee S, Sil PC. *The beneficial role of curcumin on inflammation, diabetes and neurodegenerative disease: a recent update.* Food Chem Toxicol. 2015;83:111–124. doi:10.1016/j.fct.2015.05.022.
29. Müller RH, Radtke M, Wissing SA. *Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) in cosmetic and dermatological preparations.* Adv Drug Deliv Rev. 2002;54 Suppl 1:S131–S155. doi:10.1016/S0169-409X(02)00118-7.
30. Naseri N, Valizadeh H, Zakeri-Milani P. *Solid lipid nanoparticles and nanostructured lipid carriers: structure, preparation and application.* Adv Pharm Bull. 2015;5(3):305–313. doi:10.15171/apb.2015.043.
31. Patel MR, Patel RB, Parikh JR, Patel BG. *Novel nanoemulsion-based gel formulation of tazarotene for targeted therapy of acne: formulation, characterization and comparative clinical evaluation.* Int J Pharm. 2016;523(1):1–14. doi:10.1016/j.ijpharm.2017.03.028.
32. Govindarajan VS. *Turmeric—chemistry, technology, and quality.* Crit Rev Food Sci Nutr. 1980;12(3):199–301. doi:10.1080/10408398009527278.
33. Müller RH, Radtke M, Wissing SA. *Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) in cosmetic and dermatological preparations.* Adv Drug Deliv Rev. 2002;54 Suppl 1:S131–S155.
34. Calvo P, Remuñán-López C, Vila-Jato JL, Alonso MJ. *Novel hydrophilic chitosan–polyethylene oxide nanoparticles as protein carriers.* J Appl Polym Sci. 1997;63(1):125–132.
35. Danaei M, Dehghankhold M, Ataei S, et al. *Impact of particle size and polydispersity index on the clinical applications of lipidic nanocarrier systems.* Pharmaceutics. 2018;10(2):57. doi:10.3390/pharmaceutics10020057.
36. Huang X, Brazel CS. *On the importance and mechanisms of burst release in matrix-controlled drug delivery systems.* J Control Release. 2001;73(2–3):121–136. doi:10.1016/S0168-3659(01)00248-6.
37. Mohanty C, Sahoo SK. *The in vitro stability and in vivo pharmacokinetics of curcumin prepared as an aqueous nanoparticulate formulation.* Biomaterials. 2010;31(25):6597–6611. doi:10.1016/j.biomaterials.2010.04.062.
38. Dash S, Murthy PN, Nath L, Chowdhury P. *Kinetic modeling on drug release from controlled drug delivery systems.* Acta Pol Pharm. 2010;67(3):217–223.
39. Jain S, Tiwary AK, Sapra B, Jain NK. *Formulation and evaluation of ethosomes for transdermal delivery of lamivudine.* AAPS PharmSciTech. 2007;8(4):E111. doi:10.1208/pt0804111.
40. Morton JJ, Malone MH. *Evaluation of vulnerary activity by an open wound procedure in rats.* Arch Int Pharmacodyn Ther. 1972;196(1):117–126.
41. Eddy NB, Leimbach D. *Synthetic analgesics. II. Dithienylbutenyl- and dithienylbutylamines.* J Pharmacol Exp Ther. 1953;107(3):385–393.