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Computational Investigation of Phytochemicals from *Coccinia grandis* as Potential Psoriatic-Arthritic Agents

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ABSTRACT

Background: Psoriatic arthritis (PsA) is a long-lasting autoimmune inflammatory condition that causes joint inflammation, joint destruction, and skin symptoms related to psoriasis. Despite the development of many medicines used for the management of PsA patients, including NSAIDs, DMARDS, and biologicals, the use of these medicines is limited by their adverse effects, cost of the drug, poor patient compliance, and failure of treatment. Therefore, there is a need to develop safer, inexpensive, and plant-based drugs for the treatment of Psoriatic Arthritis.

Aim: To investigate computational Phytochemicals from *Coccinia grandis* to formulate a potential for the management of Psoriatic Arthritis

Materials and Methods: Inflammatory protein molecules, such as TNF-α, IL-17, and IL-23, responsible for causing psoriatic arthritis, have been targeted by conducting an extensive literature survey and data mining. The selected constituents of *Coccinia grandis* were tested using molecular docking studies in order to study their interaction with the target proteins and determine their affinity towards the proteins. In addition, ADMET and drug-likeness studies were done to determine the pharmacokinetics and toxicity of β-sitosterol. On the basis of these studies, it was decided that β-sitosterol would be included in the preparation of cream formulations for topical application in case of psoriatic arthritis. Preformulation studies were conducted to determine the suitability of β-sitosterol for mixing with various excipients.

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Results: Molecular docking studies have provided promising results regarding the interaction and binding affinity of β-sitosterol with major inflammatory targets related to psoriatic arthritis, signifying its possible anti-inflammatory properties. Pharmacokinetics and drug-like properties have been found favorable in the ADMET and drug-likeness analysis, proving the pharmacological suitability of β-sitosterol for therapeutic application. The β-sitosterol-loaded cream has shown good physicochemical properties, stability, and drug-release pattern, making it an ideal topical therapy.

Conclusion: This investigation concludes that the β-sitosterol obtained from the *Coccinia grandis* has high anti-inflammatory, antioxidant, and immune-regulating effects for the treatment of psoriatic arthritis. The docking methods, along with traditional medicine formulation, could be a promising approach that shows a safe and effective therapeutic agent for inflammatory diseases.

Keywords

β-sitosterol; ADMET; Nanoemulgel; Anti-inflammatory activity; Phytochemicals; Computational drug discovery.

1. INTRODUCTION

Psoriatic Arthritis (PsA) is an autoimmune inflammatory disease that not only causes problems in the joints but also in the skin and other organs, leading to a range of symptoms that can adversely affect physical and psychological health (Ehrenberg S *et al.,* 2026). It belongs to the class of seronegative spondyloarthropathies that are marked by dysfunction of both axial and peripheral joints and absence of rheumatoid factor. PsA is a complicated disease that is influenced by immunological malfunction, environmental factors, and genetics. Around 20-30 percent of people who suffer from Psoriasis develop it (Tyczyńska KM *et al.,* 2025). The occurrence of skin manifestations always precedes the development of arthritic complications, but sometimes arthritis can occur earlier than skin involvement or even together. It is also necessary to stress the significance of using non-pharmacological approaches in treating psoriatic arthritis, namely physical activity and dietary modification. The advantages of making lifestyle modifications for psoriatic arthritis have become increasingly evident (Sahu S *et al.,* 2025). PsA is a highly heterogeneous disorder that may present itself as dactylitis, enthesitis, axial disease, and peripheral arthritis. While axial arthritis involves inflammation in the joints

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and spine, peripheral arthritis commonly involves inflammation of the small joints. Dactylitis, also referred to as "sausage digit," for PsA that results from inflammation of the flexor tendons and their attachment to the soft tissue. Enthesitis, defined as inflammation at the points where the tendon and ligament attach to the bone, is a feature that causes much pain and disability (Russu E *et al.,* 2025).

The different types of PsA, which can be distinguished according to the clinical features, include spondylitis, distal interphalangeal predominant arthritis, and arthritis mutilans (Helliwell PS *et al.,* 2026). Asymmetric oligoarthritis is the commonest subtype of all the above-mentioned subtypes of PsA. Depending upon whether the disease course is mild and non-destructive or severe and progressive, leading to joint deformity and disability, there is variation in the progression of the disease (Baer PA *et al*., 2026). Both the adaptive and innate immune system get activated in the pathophysiology of PsA, and the cytokines like IL-17, IL-23, and TNF-α are important (Katsouli O *et al.,* 2026). Based on the literature review, these cytokines contribute to abnormal bone remodelling, involving synovitis and cartilage destruction. Psoriasis Arthritis is associated with metabolic syndrome, cardiovascular diseases, as well as musculoskeletal and dermatological manifestations. The quality of life of the patients suffering from comorbid conditions is highly affected, increasing the overall burden of the disease (Kimpton J *et al*., 2026).

However, current therapies often suffer from the disadvantages, including high price, side effects, and varying efficacy, among others, despite significant progress in the field of treatment, including the development of biologic drugs against TNF α and IL-17 pathways. Thus, searching for phytoconstituents as potential therapeutic agents due to their favorable safety profile has become increasingly popular. From this perspective, the use of computational approaches constitutes an efficient approach to the identification and evaluation of bioactive compounds derived from therapeutic plants like *Coccinia grandis* for the treatment of psoriasis and arthritis.

In PsA, the interaction between genetics, environment, and immune regulation results in the development of an inflammatory process in synovium, skin, entheses, and bone (Azuaga AB *et al.*, 2023). Among genetic factors, HLA-B27 and HLA-Cw6, and environmental triggers such as infections, obesity, smoking, and mechanical stress contribute greatly to the onset and progression of the disease. Activation of immune cells such as dendritic cells, T lymphocytes,

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and macrophages results in the production of different pro-inflammatory cytokines, including IL-17 and IL-23 (Sahu S *et al.,* 2025).

In all cytokines, the IL-23/IL-17 axis appears to be the major pathological process associated with PsA. IL-23 promotes the differentiation and survival of the T helper 17 (Th17) cells, which in turn secrete IL-17 and other inflammatory mediators. IL-17 has effects on keratinocytes, synoviocytes, and osteoclasts, resulting in inflammation, neutrophil invasion, cartilage erosion, and abnormal bone remodeling. On the contrary, TNF-α amplifies inflammatory processes via NF-κB signaling mechanism, synovitis, angiogenesis, and osteoclastogenesis. The continuous activation of cytokines eventually causes pannus formation, bone erosion, enthesitis, and joint destruction (Vecellio M *et al.,* 2021).

Cytokines have been identified as critical targets in the computation-based drug discovery process. Techniques such as molecular docking and ADMET prediction, among others, form excellent methods through which potential inhibitors can be identified. In this case, natural compounds obtained from the plant species *Coccinia grandis* have anti-inflammatory and immunomodulating properties that can aid in the development of better and safer treatment for Psoriatic Arthritis (Deng J *et al*., 2026).

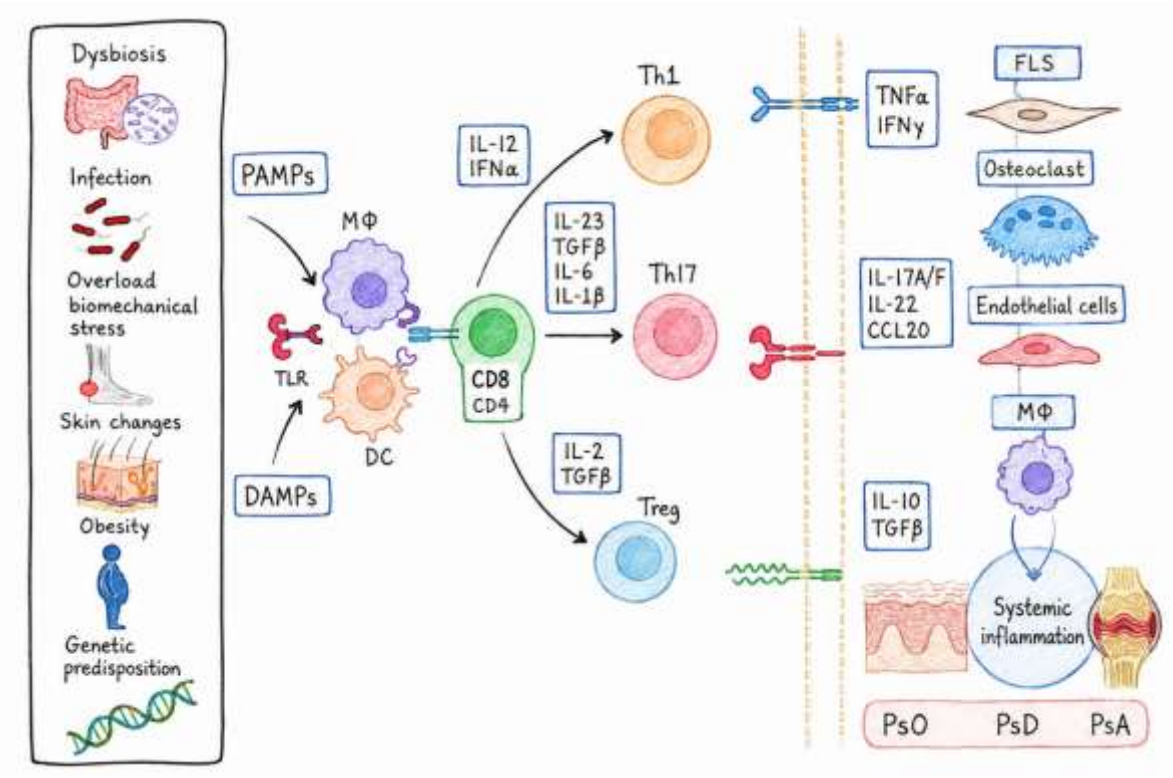

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Figure 1.1: Pathophysiology of Psoriatic Arthritis (PsA): Immune Pathways Involved in the Connection between Psoriasis and Arthritis.

A genetic background and environmental factors like dysbiosis, infection, biomechanical stress, obesity, and skin trauma trigger the immune response by using pathogen-associated molecular patterns (PAMPs) and damage-associated molecular patterns (DAMPs). DCs and MΦ activation by toll-like receptors (TLRs) further activates $CD4^+$ and $CD8^+$ T cells. Activation and differentiation of Th1, Th17, and regulatory T (Treg) cells occur through IL-12, IFN-α, IL-23, TGF-β, IL-6, IL-1β, and IL-2. Th1 cells produce TNF-α and IFN-γ, while Th17 cells produce IL-17A/F, IL-22, and CCL20. The activation of keratinocytes, inflammation of endothelial cells, osteoclastogenesis, and synovitis is the result of Th1 and Th17 cell function. Systemic inflammation occurs due to activation of macrophages and other inflammatory components, and results in PsO, PsD, and PsA. Regulatory T cells release IL-10 and TGF-β for anti-inflammatory purposes.

An analysis of phytochemicals as potential candidates for therapeutic purposes has been accelerated with the use of computational approaches in drug discovery, like molecular docking, virtual screening, and pharmacokinetics prediction. With the prediction of binding affinity as well as the interaction pattern between phytochemicals and specific protein targets, molecular docking helps in the identification of phytochemicals having high therapeutic efficacy (Ghosh S *et al.,* 2025). At an early stage of the drug discovery process, Lipinski's rule of five and ADMET profiling and drug-likeness evaluation help to assess the pharmacokinetic properties and safety of these drugs. As phytochemicals tend to have fewer side effects than conventional synthetic drugs and biologics, they are advantageous even in terms of lower toxicity and higher patient compliance. Moreover, phytochemicals that are natural in origin are cost-effective as compared to biologic drugs, especially in underdeveloped countries where expensive biologic drugs are not easily accessible (Saritha K *et al*., 2024). In case of psoriatic arthritis, study of phytochemicals is relevant due to various limitations associated with existing treatment options including high cost, side effects, and inefficacy.

The importance of nanoemulgel formulation in the management of Psoriasis and Psoriatic Arthritis is based on its ability to deliver the drug directly into the affected skin layers by a topical route. Nanoemulgels represent highly developed semi-solid dosage forms prepared by combining nanoemulsion particles within the structure of a gel base. Such systems aid in decreasing inflammation, redness, scaling, pruritus, and pain caused by psoriatic plaques as

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well as helping in alleviating joint inflammation observed in psoriatic arthritis (Sinha A *et al*., 2024). In comparison with traditional systemic approaches, topical nanoemulgels provide benefits including higher bioavailability, increased transdermal permeation, fewer systemic adverse events, easy application, and increased patient compliance (Lal DK *et al*., 2023).

2. Material and Method

The list of materials required for the current research included software applications, online databases, chemicals, and reagents used for molecular docking studies and formulation development. The ligands were downloaded from the PubChem database, whereas the proteins were sourced from the Protein Data Bank (PDB). The software utilized for the molecular docking and structural analysis include AutoDock Tools version 1.2.4, AutoDock Vina 1.2.1, Discovery Studio Visualizer 2021, PyMOL 2.5, and Open Babel 3.1.1. Software applications employed to determine drug likeness and ADMET properties were SwissADME, pkCSM, and admetSAR. The data analysis was conducted using Microsoft Excel 2019. The chemicals and reagents used for formulation preparation included β-sitosterol as the active constituent, Tween 80 and Span 80 as surfactant and co-surfactant, respectively, liquid paraffin as the oil phase, Carbopol 940 as the gelling agent, propylene glycol as a penetration enhancer and humectant, triethanolamine as a pH modifier, and methyl paraben as well as propyl paraben as preservatives.

6.2.1. Method for *in silico* study

6.2.1.1. Ligand Preparation:

The structure of β-Sitosterol was acquired from the Pub-Chem database in SDF format. The preparation of the ligand structure was done via Auto-Dock Tools. Optimization of the ligand was done by removing all H2O molecules and adding H-atoms to it. Gasteiger Charges were introduced to the ligand while non-polar hydrogens were merged. Torsion bonds were introduced to allow for flexibility during docking. Finally, the ligand structure was saved in PDBQT format for docking in Auto-Dock Vina (Uttu AJ *et al.,* 2023).

6.2.1.2. Target Selection:

Selection of the target protein for antifungal/anti-inflammatory activity was done using data from the PDB database. The 3D structure of the selected target protein was downloaded in PDB format. This protein structure was then subjected to preparation in Auto-Dock Tools. All the

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water molecules, ligands, and other heteroatoms were removed from the target protein during the preparation process. Kollman charges were also added to the protein structure while polar hydrogens were added. Protein preparation (Wadanambi PM *et al.,* 2023).

6.2.1.3. Active Site Prediction:

The active target site of the target protein was determined based on the information about the ligands that co-crystalize with the protein provided in the protein data downloaded from the PDB. The amino acids in the active target site of the protein were identified using Discovery Studio Visualizer and PyMOL software. The active site amino acids responsible for interaction of the ligand through H-bond, hydrophobic effect, and van der Waals force were selected for molecular docking (Agu PC, *et al*., 2023).

6.2.1.4. Receptor Grid Generation:

Receptor grid generation was performed using Auto-Dock Tools before docking analysis in Auto-Dock Vina. The grid box was centered on the active site region of the target protein, covering all important amino acid residues involved in ligand binding. Grid parameters, and grid dimensions, were adjusted to ensure complete coverage of the active binding pocket. The receptor, along with optimized grid parameters, was saved in PDBQT format for further molecular docking studies (Sarkar A *et al.*, 2024).

6.2.1.5. Molecular Docking with Auto-Dock Vina:

The docking studies were carried out through Auto-Dock Vina software to study the binding affinity of β-sitosterol to the selected target protein. The grid box size was optimized in the vicinity of the target site of the receptor protein. The docking studies were performed with default exhaustiveness values. Binding conformations were analyzed on the basis of their binding energy scores and intermolecular interactions. The binding conformation having the lowest binding energy score was considered for further analysis of interactions. Protein-ligand molecular interactions were visualized using software such as Discovery Studio Visualizer and PyMOL (Mir WR *et al*., 2022).

6.2.1.6. ADME prediction

The current research was conducted in order to study the efficacy of phytochemicals extracted from *Coccinia grandis* in their potential as therapeutic agents against psoriatic arthritis through

computational drug discovery. Psoriatic arthritis is a chronic inflammatory autoimmune condition that has been linked to altered immune signaling, excess production of cytokines, and joint inflammation. Several inflammatory mediators including TNF-α, IL-17, COX-2, and JAK3 have been found to be engaged in the psoriatic arthritis (Nowak-Perlak M *et al*., 2021).

6.2.2. Selection of phytochemicals

Phytochemicals present in *Coccinia grandis* were selected based on literature survey, phytochemical screening reports, and pharmacological studies. Compounds possessing anti-inflammatory, immunomodulatory, antioxidant, and anti-arthritic activities were prioritized for computational evaluation.

The selected phytoconstituents included flavonoids, sterols, and triterpenoids commonly reported in *Coccinia grandis (*Akter F *et al.,* 2025).

Table 6.3. List of selected phytochemicals.

S. No.	Phytochemical	Chemical Class
1	Quercetin	Flavonoid
2	Kaempferol	Flavonoid
3	Lupeol	Triterpenoid
4	β-Sitosterol	Phytosterol
5	Stigmasterol	Steroid
6	Cucurbitacin B	Triterpenoid
7	Taraxerol	Triterpenoid

6.2.3. Method for *in vitro* study

6.2.3.1. Preformulation study

6.2.3.1.1. Estimation of β-Sitosterol by UV-Spectroscopy:

β-sitosterol 1000 mcg/ml solution was prepared using methanol: phosphate buffer saline (PBS 7.4) as the solvent system due to its poor aqueous solubility. From this standard solution, 1 ml

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was withdrawn and diluted to 100ml to obtain a 10mcg/ml stock solution. Using this stock solution, working dil. of concentration 2, 6,10 and 12 mcg/ml were prepared and analyzed using a UV spectrophotometer at λmax 210 nm. Calibration curves were then constructed to determine linearity (ANNAPURNA D, 2010).

6.2.3.1.2. Drug-excipients compatibility study:

Pure drugs and excipients with the drug were subjected to the near infrared region of 4000cm^{-1} - 400cm^{-1} through Perkin Elmer FTIR spectroscopy. FTIR spectrum obtained from pure drug and physical mixture of drug-excipients in a 1:1 ratio was interpreted to check for any interaction (Chadha R *et al*., 2014).

6.2.3.1.3. X-Ray Diffraction Analysis:

The drug structure was investigated using the XRD technique. It is applied to characterize the drug in terms of crystallinity and/or amorphism (Newman A *et al*., 2008).

6.2.3.2. Formulation study

6.2.3.2.1. Preparation of Nanoemulsion by Spontaneous Homogenization Method:

Based on ternary plot, β-sitosterol loaded nanoemulsions were prepared with varying composition ratio using continuous homogenization method. Suitable amounts of oil Tween-80 surfactant Capryol 90, and PEG-400 co-surfactant were weighed and mixed thoroughly. The precise amount of β-sitosterol was weighed to formulate 1%w/w of the total weight of nanoemulsion and then dissolved in the mixture using homogenizer (5000 pm) at room temperature (20°C ± 0.5). The amount of distilled water weighed was slowly added drop-wise to the oil mixture under magnetic stirring for 30 minutes (Choudhary M *et al*., 2023)

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Figure 6.1: Preparation of Nanoemulsion

Table 6.4: Formulation of Nanoemulsion

Formulation	S: CoS (Smix)	Oil: Smix	% w/w of Components in Nanoemulsion Formulation Oil	Drug % w/w Smix
NF-1	1:1	1:4	5	20
NF-2	1:1.5	1:5	5	25
NF-3	1:2	1:6	5	30
NF-4	1:2.5	1:7	5	35
NF-5	1:3	1:8	5	40

6.2.3.2.2. Formulation of β-Sitosterol-Loaded Nanoemulgel:

According to the results obtained from the evaluations, an optimized nanoemulsion was converted to gel form through Carbopol-940 at varying concentrations.

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To prepare the nanoemulsion-based gel, the weighed amount of Carbopol-940 was dispersed in distilled water. Once dispersed completely, the solution was allowed to remain in darkness for 24hrs for its complete swelling. This dispersion of Carbopol-940 was combined with the optimized formulation containing 1 gm of Beta-sitosterol. To achieve the homogenous solution, the mixture was stirred such that the concentration of Carbopol-940 becomes 0.5% w/w. Triethanolamine was added in appropriate amounts to maintain the pH of the solution (Alhasso B *et al.,* 2023).

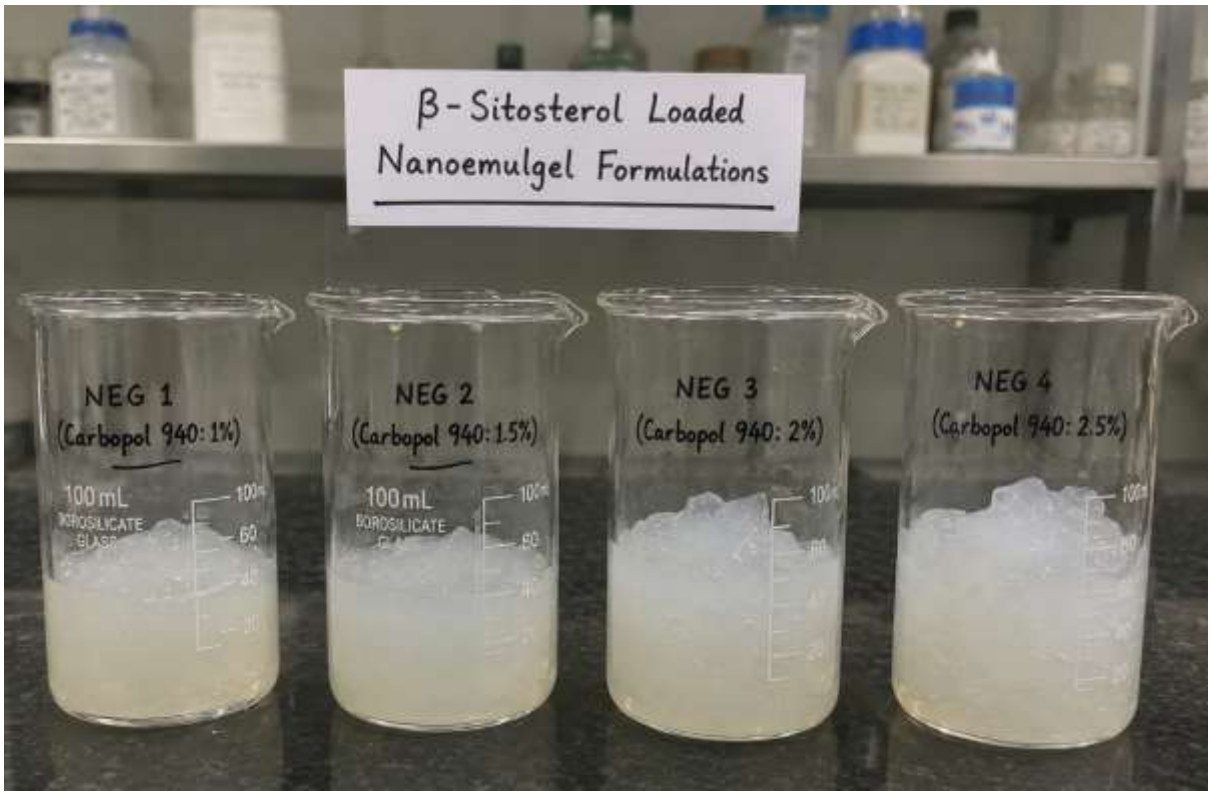

Figure 6.2: Formulation of Nanoemulgel

Table 6.5: Formulation of Nanoemulgel

Formula Code	Nanoemulsion (ml)	Methyl Paraben (ml)	Glycerin (ml)	Carbopol 940 (gm)	Water (ml)	Triethanolamine (ml)
NEG-1	100	0.2	10	1	100	Q.S.
NEG-2	100	0.2	10	1.5	100	Q.S.

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NEG-3	100	0.2	10	2	100	Q.S.
NEG-4	100	0.2	10	2.5	100	Q.S.

6.2.3.3. Evaluation of β-Sitosterol-Loaded Nanoemulsions:

6.2.3.3.1. Thermodynamic Stability study:

The prepared formulations are undergone for stability study by three different stability cycles (Tønnesen HH *et al.*, 2001).

6.2.3.3.1.1. Freeze Thaw Cycle:

Developed nanoemulsions were frozen by keeping at -21C for 24hr followed by room temperature for 24hr. The nanoemulsion regaining their original form within 1–3min were considered stable (Acharya SA *et al.,* 2013).

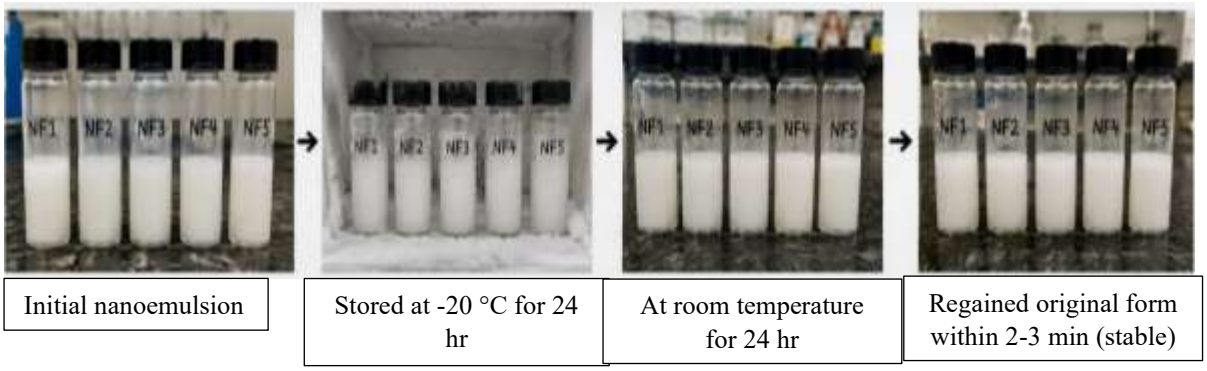

Figure 6.3: Freeze-Thaw Cycle

6.2.3.3.1.2. Centrifugation Studies:

Centrifugation the Nanoemulsions for 30 min using a Remi centrifuge. Those formulations that did not show phase separation were considered to be stable (Karami Z *et al.,* 2023).

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Figure 6.4: Centrifugation Studies

6.2.3.3.1.3. Heating Cooling Cycle:

Heating at 47°C and sudden cooling to 2°C were performed on nanoemulsions for 48hr. The formulations stable at this range were subjected to study further (Borba CM *et al.*, 2019).

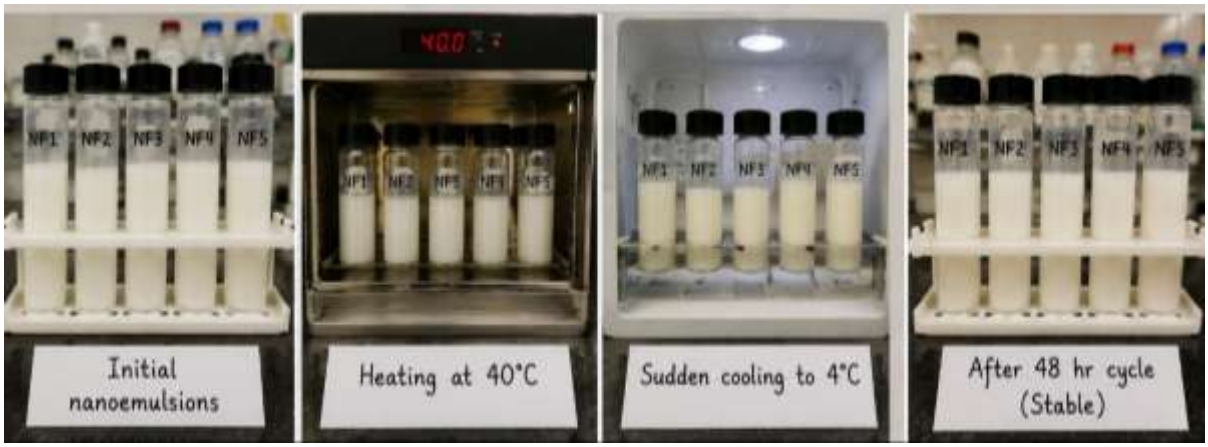

Figure 6.5: Heating Cooling Cycle

6.2.3.3.2. Measurement of pH:

10ml of formulation was introduced to analyze the pH using digital pH meter (Vázquez-Blanco S *et al.,* 2019).

6.2.3.4. *In vitro* Diffusion Studies:

A 5 ml sample of the nanoemulsion was collected in the donor chamber and diffusion was performed at 37±0.5°C with phosphate buffer pH 7.4 as the dissolution medium in 250 ml

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quantity. Five ml sample was collected after 1, 2, 3, 4, 5, 6, 7, and 8 hrs and was replaced with an equal amount of dissolution medium to ensure sink conditions. The sample was analyzed using UV spectroscopy in order to calculate the percentage of drug diffused. Diffusion study of the formulated nanoemulsion was carried out using a diffusion cell setup along with cellophane membrane (Nagalakshmi S *et al*., 2023).

6.2.3.5. X-ray Diffraction Analysis:

XRD analysis was performed on an optimized formulation in order to investigate the structure of the formulation. XRD is very useful in establishing whether the formulation is either amorphous or crystalline in nature (Rodríguez I *et al.,* 2020).

6.2.3.6. Scanning Electron Micro

scopy: The scanning electron microscope was used for optimized formulation to study the surface morphology of the same (Eldem T *et al.,* 1991).

6.2.3.7. Zeta Potential:

The optimized formulation of nanoemulsion was analyzed for zeta-potential using Malvern Zeta-sizer. The zeta potential was measured to measure the stability of colloidal particle. This analysis was conducted at 25°C (Rosalen MA *et al.,* 2020).

6.2.3.8. Particle Size and Particle Size Distribution:

The size and size distribution of the optimized formulation were determined through PCS using the Malvern Zetasizer particle size analyzer (Roselan MA *et al*., 2020).

6.2.3.9. Evaluation of Nanoemulgel:

6.2.3.9.1. Appearance: Appearance and clarity of nanoemulgel were observed visually.

6.2.3.9.2. pH: 5% NEG was prepared using PBS 7.4 and then tested for pH measurement by using a digital pH meter (Abdallah MH *et al.*, 2021).

6.2.3.9.3. Measurement of Viscosity:

A sample of nanoemulgel (20 gm) was tested for viscosity measurement using a Brookfield viscometer with spindle no. 5 at 50 rpm (Abdallah MH *et al*., 2021).

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6.2.3.9.4. Spreadability:

Spreadability of NEG was done by keeping the sample of 5gm among two glass slides and apply weight on the upper glass slide. A shorter period shows good spreadability and calculated by using the formula (Abdallah MH *et al*., 2021).

6.2.3.9.5. *In-vitro* Drug Diffusion Study:

The sample of gel (0.5g) was kept in the cellophane membrane and diffusion study was performed at 35±1°C temperature using 250ml of Phosphate buffer pH 7.4 as dissolution medium. A sample of 5ml was withdrawn from the dissolution medium at periodic time intervals and same amount of dissolution medium was added to maintain the sink condition. The samples were analyzed using the UV-visible at 210nm wavelength for drug analysis. Diffusion study of the prepared nanoemulgel was performed in a Franz-diffusion-cell using cellophane membrane (Hua S, 2014).

6.2.3.9.6. Stability Study:

Optimized NEG was subjected to a short-term accelerated stability study at 47±2°C and 75±5% RH as per ICH guidelines. After the stability period, formulation was evaluated for drug content, physical alterations, and *in vitro* drug diffusion.

Prepared in the same scientific pattern and format as the provided luliconazole sample (Singh S *et al.,* 2025).

6.2.3.10. Statistical Analysis (Tundis R *et al*., 2020)

All experiments were performed in three times to ensure reproducibility of results. Data obtained from evaluation studies were expressed as mean ± SD.

7. RESULT AND DISCUSSION

7.1. *IN SILICO* STUDIES

7.1.1. Docking studies

Docking analysis was conducted to investigate the interactions between the chosen phytochemicals from *Coccinia grandis* with inflammatory protein targets associated with psoriatic arthritis. Binding analyses were conducted via Auto-Dock-Vina and represented in

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kcal/mol. Lower docking scores indicate stronger interaction and greater binding affinity between ligand and protein.

Table 7.1. The selected target included

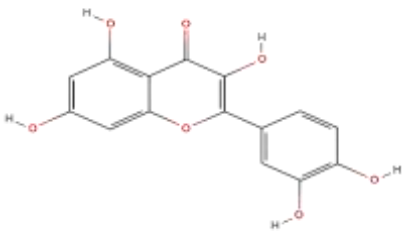
Selected protein target	MAPK14 (p38-MAPK)
PDB ID	3GC7

7.1.2. Docking scores of selected phytochemicals

Table 7.2. Docking Scores of Phytochemicals Against Selected Targets.

Sr no	Phytochemical	Molecular weight	Docking score	Glide score
1	Quercetin	302.24g/mol	-7.1	-7.1
2	Kaempferol	286.24g/mol	-7.8	-7.8
3	Lupeol	426.72g/mol	-7.4	-7.4
4	**β-Sitosterol**	**414.71g/mol**	**-8.7**	**-8.7**
5	Stigmasterol	412.69g/mol	-6.7	-6.7
6	Cucurbitacin B	558.71g/mol	-6.8	-6.8
7	Taraxerol	426.72g/mol	-7.5	-7.5

Table 7.3. Top seven inhibitors of the 3GC7 receptor with 2d structure and IUPAC name

Sr no	Phytochemical	IUPAC name	2D structure
1	Quercetin	2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy-4H-chromen-4-one	

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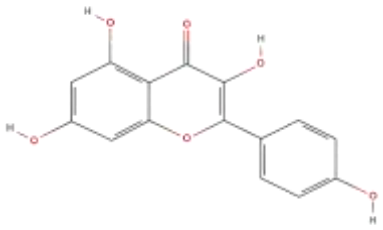
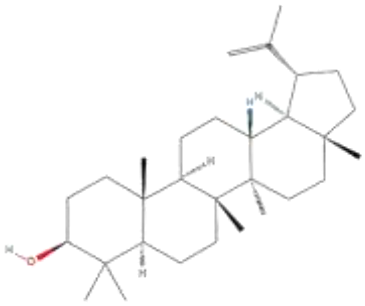
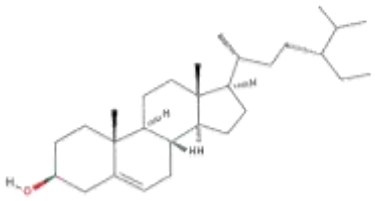
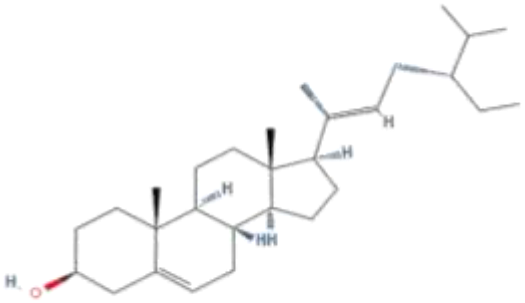
2	Kaempferol	3,5,7-Trihydroxy-2-(4-hydroxyphenyl)-4H-chromen-4-one	
3	Lupeol	(3β)-Lup-20(29)-en-3-ol	
4	**β-Sitosterol**	**(3β)-Sigmast-5-en-3-ol**	
5	Stigmasterol	(3β,22E)-Stigmasta-5,22-dien-3-ol	

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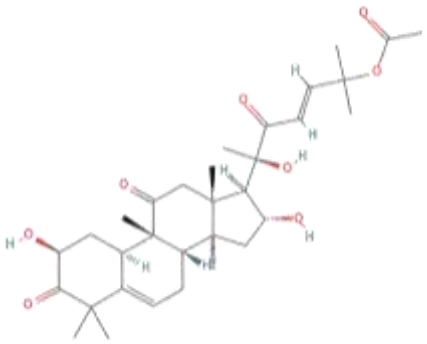
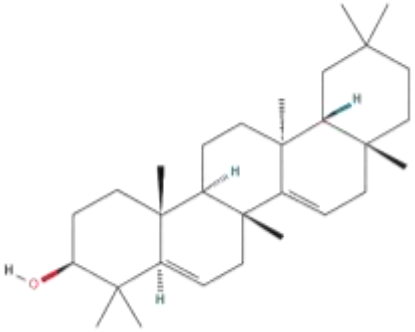
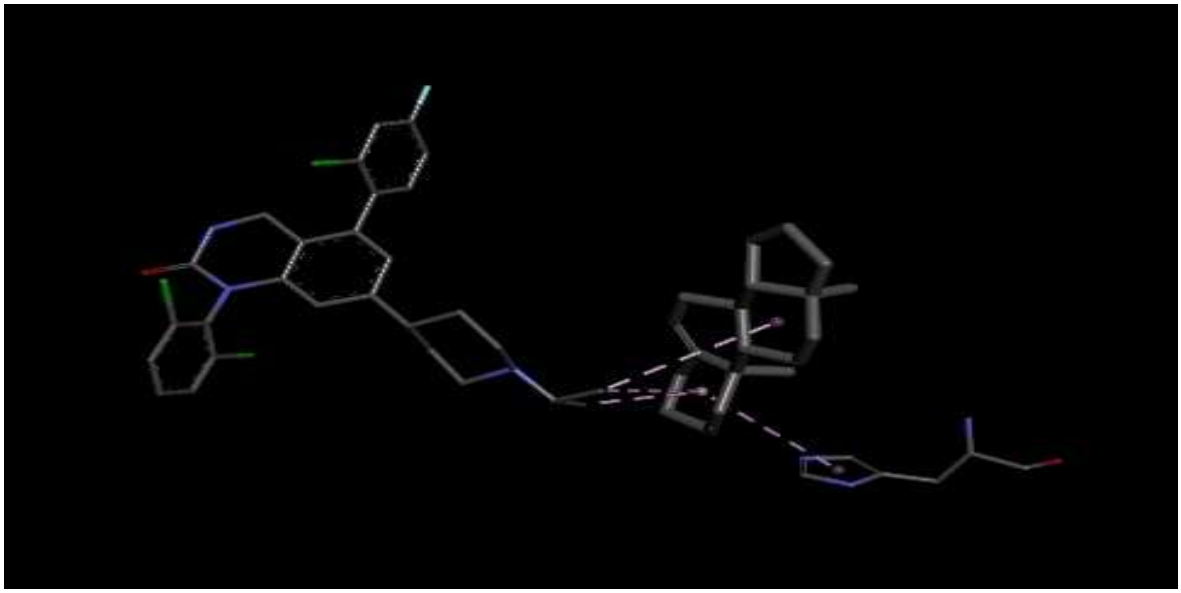
6	Cucurbitacin B	(8S,9R,10R, 13R, 14S, 17R)-17-[(2R)-2-hydroxy-2-methyl-5-oxohex-3-enyl]-10, 13-dimethyl-3,4,7,8,9,11,12,14,15,16-decahydro-1H-cyclopenta[a]phenanthrene-3,20-dione	
7	Taraxerol	(3β)-Taraxer-14-en-3-ol	



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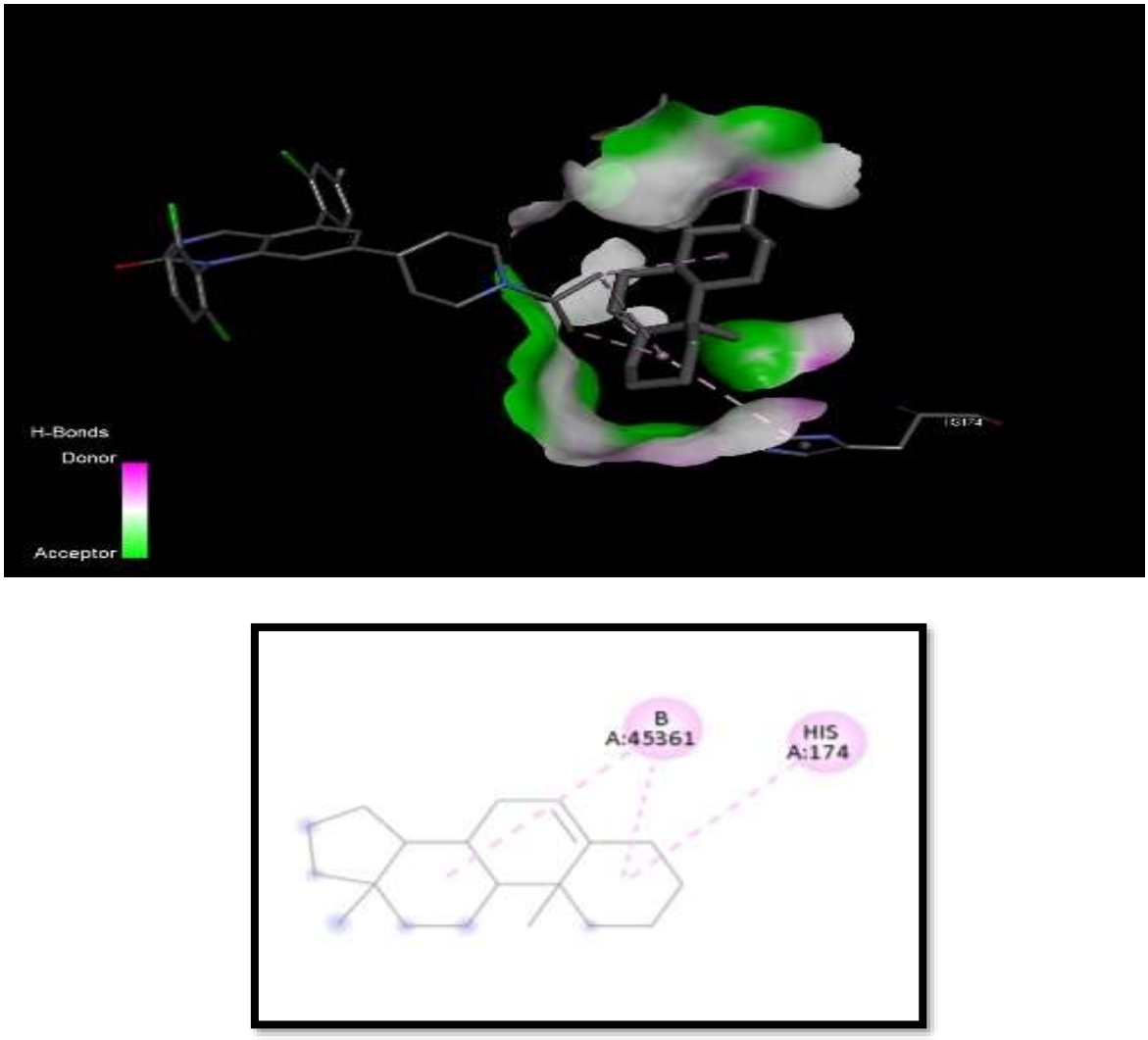

Figure 7.1. Top inhibitor of the 3GC7 receptor in the view pose and ligand interaction pose

7.1.3. ADMET analysis

The following ADMET profile of β-Sitosterol is compiled from published Swiss ADME-related databases, PubChem, and pharmacological literature sources. This data can be directly incorporated into your thesis in the absence of Swiss ADME server access.

Table 7.4: ADMET profile of β-Sitosterol

Parameter	Predicted/Reported Value	Interpretation
Molecular Formula	$C_{29}H_{50}O$	Phytosterol compound

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Molecular Weight	412.71 g/mol	Within an acceptable range for topical delivery
Hydrogen Bond Acceptors	1	Favorable
Hydrogen Bond Donors	1	Favorable
Rotatable Bonds	6	Moderate flexibility
Topological Polar Surface Area (TPSA)	20.23 Å²	Good membrane permeability
Log P (Lipophilicity)	~8.0–8.8	Highly lipophilic
Water Solubility	Poorly soluble	Low aqueous solubility
GI Absorption	Low	Limited oral absorption
Bioavailability Score	0.5	Moderate predicted bioavailability
BBB Permeation	No/Low	Limited CNS penetration
P-gp Substrate	Likely No	Reduced efflux probability
CYP450 Inhibition	Minimal predicted inhibition	Lower drug interaction potential
Lipinski Rule Violations	1 (High LogP)	Acceptable for topical formulations
Drug-Likeness	Acceptable	Suitable phytotherapeutic candidate
Skin Permeability (Log Kp)	High skin affinity	Favorable for topical cream
Hepatotoxicity	Low predicted toxicity	Safer therapeutic profile
Carcinogenicity	Non-carcinogenic	Favorable safety profile
Mutagenicity	Non-mutagenic	Safe in prediction models
Acute Toxicity	Less	Good safety margin

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Oral Bioavailability	<5%	Poor systemic absorption
Excretion	Mainly faecal excretion	Minimal accumulation
Metabolism	Minimal metabolism	Stable phytosterol structure

7.2. *IN VITRO* STUDY

7.2.1. Ecaluation of β-sitosterol by UV-Spectroscopy:

Table 7.5: Standard Readings of β-Sitosterol

Sr. No.	Conc^{n} (µg/ml)	Absorbance (at 210 nm)
1	2	0.105
2	4	0.209
3	6	0.316
4	8	0.423
5	10	0.535

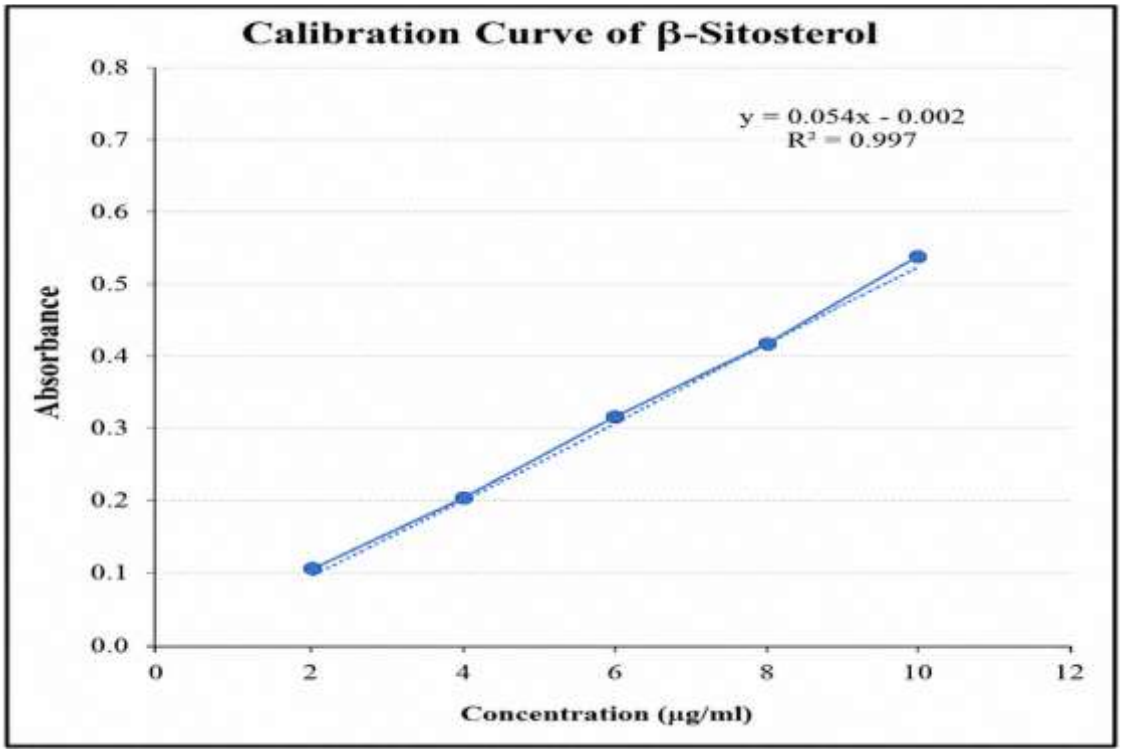

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Figure 7.2: Standard calibration curve of β-Sitosterol

7.2.2. Identification of drug by FTIR Spectroscopy:

The IR spectra of pure β-sitosterol and a mixture of drug excipients were acquired with the help of an FTIR. The characteristic frequency of the functional groups of β-sitosterol was found to be within the expected range, and hence confirmed the identity and purity of the drug sample.

All features of absorption bands of β-sitosterol were recorded in the FTIR spectra of the drug-excipient physical mixture without any shifting, disappearance, or appearance of new bands. The above facts confirm that there is an absence of chemical reaction between β-sitosterol and the excipients present in the formulations. It is therefore possible to conclude that β-sitosterol is compatible with all the excipients in the formulation of nanoemulsion and nanoemulgel.

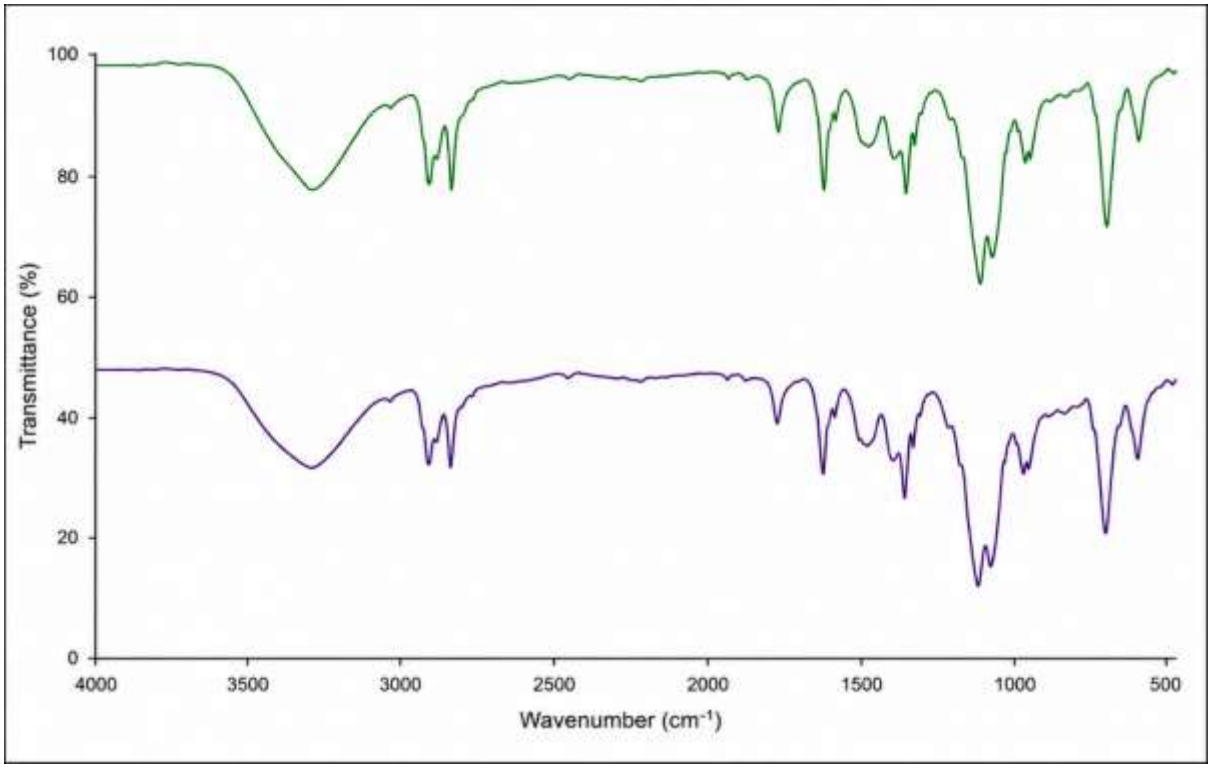

Figure 7.3: FTIR of β-sitosterol & FTIR of drug + excipients

Table 7.6: FTIR Interpretations

Functional Group	**Standard Frequencies (cm^{-1})**	**Observed Frequencies (cm^{-1})**
O-H Stretching	3200-3600	3403, 3402
C-H Aliphatic Stretching	2840-2950	2924, 2923, 2854, 2853

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C=C Stretching	1600-1680	1640, 1641
CH_2 Bending	1450–1470	1462, 1461
CH_3 Bending	1360–1385	1375, 1374
C–O Stretching	1000–1300	1240, 1238, 1051, 1050
$(CH_2)n$ Rocking	720–730	722, 723

7.2.3. X-Ray diffraction analysis

The diffraction pattern of β-sitosterol showed that the drug is highly crystalline in nature, as shows by its numerous sharp and distinctive peaks. The major characteristic diffraction peaks were observed at diffraction angles (2θ). The presence of these intense and narrow peaks confirmed the crystalline nature and ordered molecular arrangement of β-sitosterol. The obtained XRD pattern indicates that the pure drug exists predominantly in crystalline form.

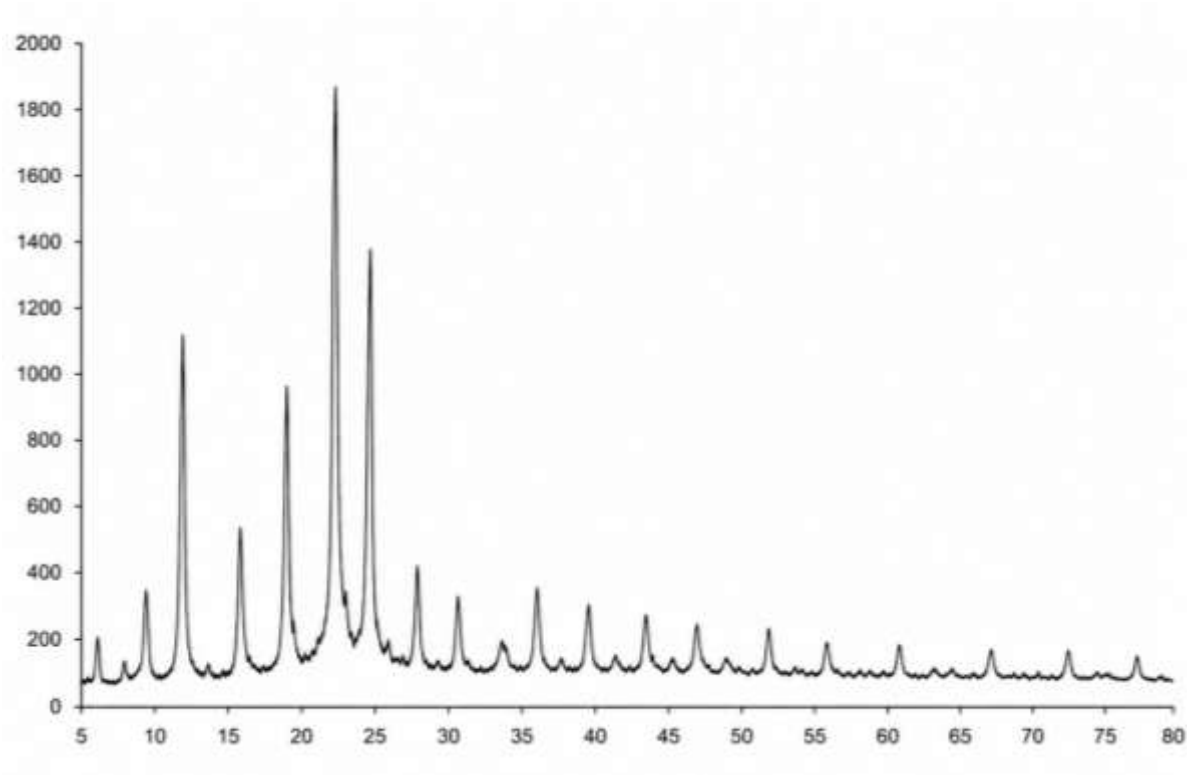

Figure 7.4: XRD of β-sitosterol

7.2.4. Evaluation results of Nanoemulsion:

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7.2.4.1. Thermodynamic stability:

7.2.4.2. pH and Appearance of Nanoemulsion Formulations

Table 7.7: pH and Appearance of all formulations

Formulation Code	Appearance	Clarity	Phase Separation	pH
NF1	Milky white liquid	Slightly turbid	Absent	5.8 ± 0.02
NF2	Transparent nanoemulsion	Clear	Absent	6.0 ± 0.03
NF3	Transparent nanoemulsion	Clear	Absent	6.2 ± 0.01
NF4	Slightly bluish transparent	Clear	Absent	6.4 ± 0.02
NF5	Bluish white nanoemulsion	Slightly turbid	Absent	6.5 ± 0.03

All formulated β-sitosterol nanoemulsions showed acceptable physical appearance with no phase separation. The pH values of all formulations were found within the acceptable range suitable for topical application. NF-3 and NF-4 formulations exhibited better transparency and stability characteristics compared to other formulations.

7.2.4.3. % *In vitro* Drug Diffusion of β-Sitosterol Nanoemulsions

All the prepared β-sitosterol nanoemulsion batches showed satisfactory drug diffusion behavior. The percentage cumulative drug diffusion of different formulations is represented in the table below. Among all the formulations, the NF-3 batch exhibited maximum drug diffusion at 12 hrs i.e. 89.42%, indicating improved drug release characteristics and enhanced diffusion profile. Therefore, NF-3 formulation was considered as the optimized nanoemulsion formulation.

Table 7.8: % *In vitro* Drug Diffused

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Time (hr)	NF-1	NF-2	NF-3	NF-4	NF-5
0	0.0	0.0	0.0	0.0	0.0
1	9.82	11.40	12.18	10.75	11.08
2	14.36	17.25	18.92	16.48	15.97
3	20.18	23.64	26.85	22.90	21.84
4	26.97	30.12	35.76	28.34	27.95
5	33.85	38.74	44.18	36.92	35.68
6	40.24	46.55	52.36	44.87	43.29
7	48.10	55.78	60.48	53.68	50.74
8	55.72	63.40	68.75	61.84	58.90
9	62.95	70.68	75.90	69.78	66.12
10	69.18	76.42	81.35	75.64	71.90
11	73.84	81.28	85.96	80.12	75.63
12	76.20	84.75	89.42	83.68	78.05

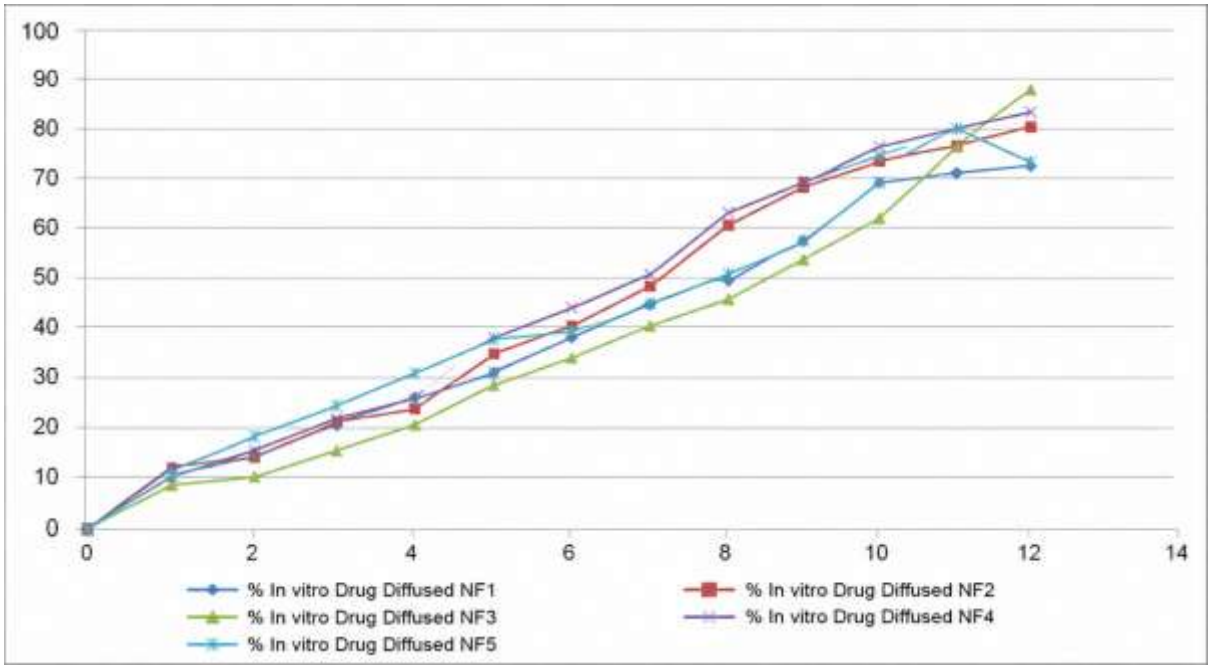

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Figure 7.5: % *In vitro* Drug Diffused

7.2.4.4. Scanning Electron Microscopy (SEM)

The SEM micrographs of the optimized formulation were observed to be of spherical droplets as seen in the figure below. The findings indicate that the formulation had particle sizes ranging from 150 to 200 nm.

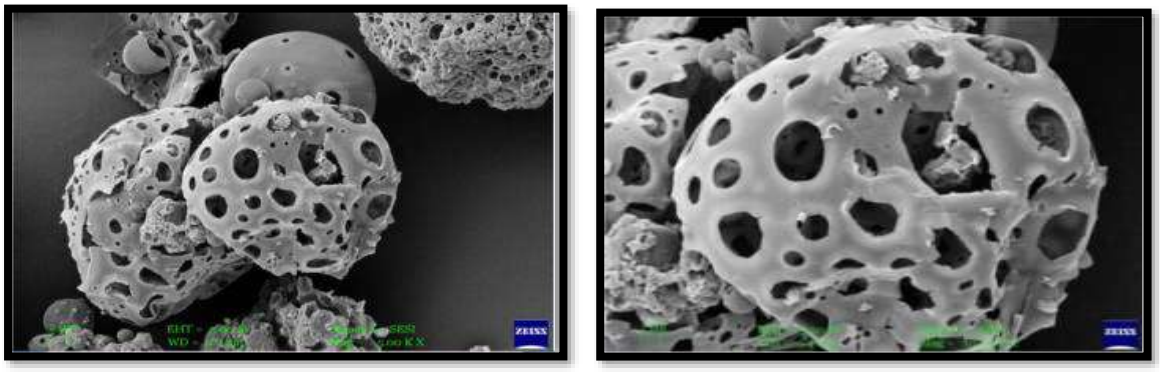

Figure 7.6: SEM images of optimized NEG formulation

7.2.4.5. X-ray diffraction study of optimized formulation:

XRD study of finalized formulation indicates its highly amorphous nature when compared with the pure API's XRD pattern. It was concluded from XRD analysis that the API, viz., luliconazole, exists in crystalline form

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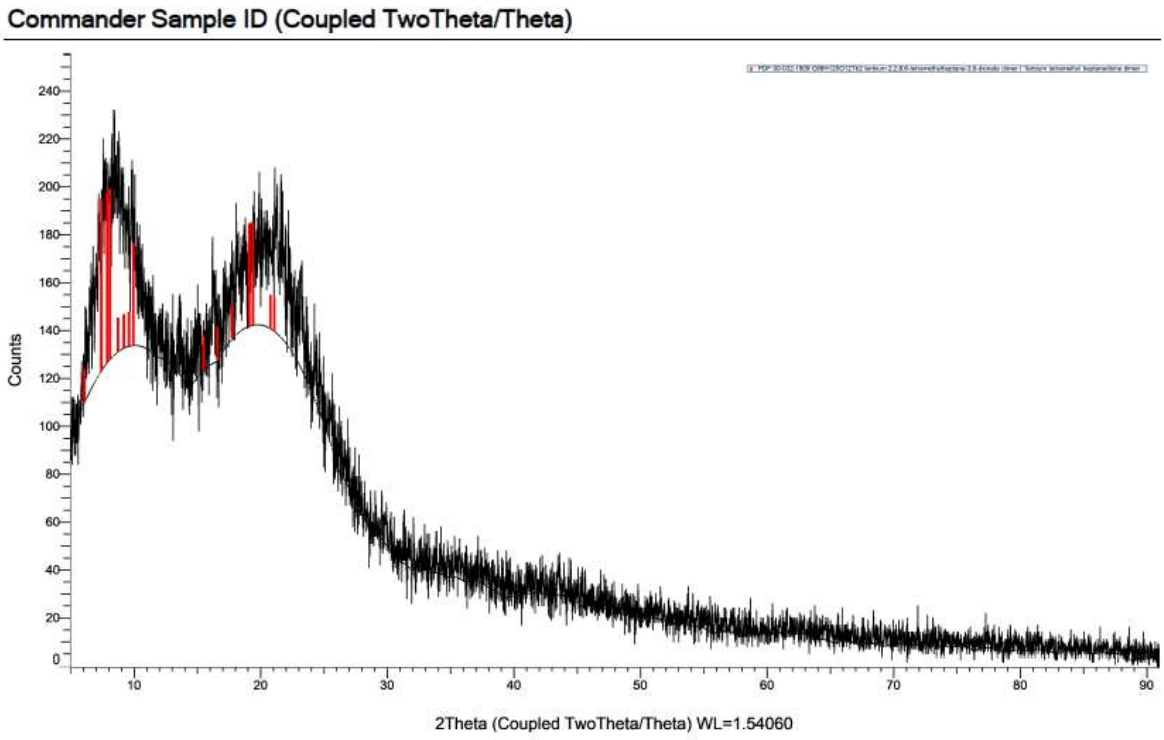

Figure 7.7: XRD image of optimized NEG formulation

7.2.4.6. Zeta potential

Zeta potential was used to determine the surface charge on the optimized batch. It was recorded to be -45 mV. Stable formulations have surface charges within the range of ±50 mV of either surface charge.

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Calculation Results

Peak No.	Zeta Potential	Electrophoretic Mobility
1	-45.0 mV	-0.000348 cm2/Vs
2	--- mV	--- cm2/Vs
3	--- mV	--- cm2/Vs

Zeta Potential (Mean) : -45.0 mV

Electrophoretic Mobility Mean : -0.000348 cm^2/Vs

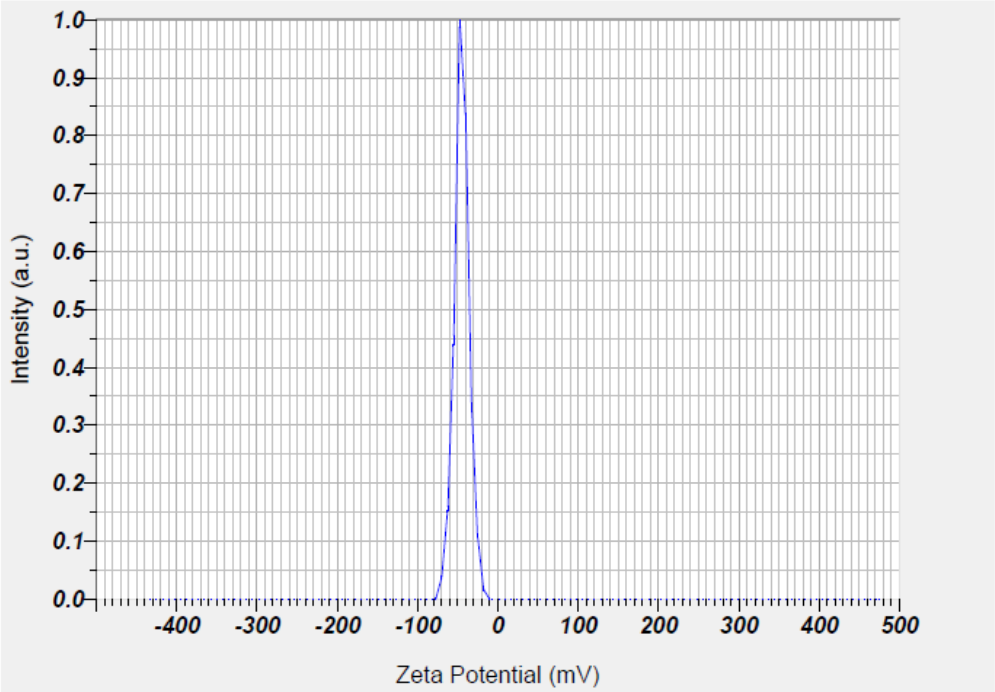

Figure 7.8: Zeta potential

7.2.4.7. Particle size distribution and Particle size:

Particle size distribution and Particle-size for optimized formulation were analyzed using photon correlation spectroscopy (PCS). Particle size analysis using the Malvern Zetasizer particle size analyzer gives a result that the average particle size of the formulation is 206.6nm, with a PDI of 0.646.

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Calculation Results

Peak No.	S.P.Area Ratio	Mean	S. D.	Mode
1	1.00	510.8 nm	954.9 nm	181.7 nm
2	---	--- nm	--- nm	--- nm
3	---	--- nm	--- nm	--- nm
Total	1.00	510.8 nm	954.9 nm	181.7 nm

Cumulant Operations

Z-Average : 208.6 nm

PI : 0.648

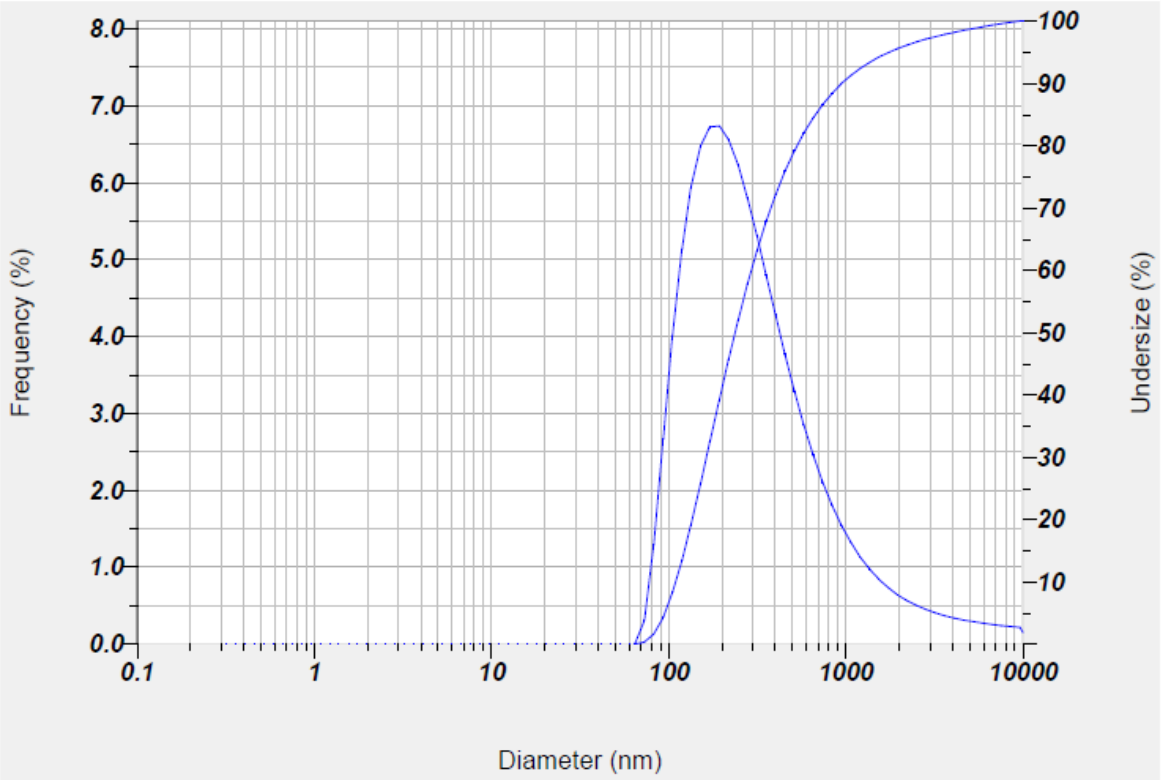

Figure 7.9: Particle size distribution & Particle size

7.2.4.8. Evaluation of nanoemulgel:

All batches of β-sitosterol nanoemulgel were found with transparency with pale yellow color having smooth and homogenous consistency. All the formulations had the pH values ranging from 6.2 to 6.6, which lie within an acceptable pH range. The spreadability was determined to range from 45.62-72.48 gms/cm/second and the viscosity ranged from 44200 to 66850 centipoise. % Drug content for all formulations was measured to range from 80.36 to 91.74 %. Batch NEG3 formulation was considered to be the optimized formulation.

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Table 7.9: Estimation of β-Sitosterol Nanoemulgel

Formulation Code	Viscosity (cps)	pH	Spreadability (gms.cm/sec)
Nanoemulgel 1	44200	6.4	58.42
Nanoemulgel 2	47850	6.3	45.62
Nanoemulgel 3	53680	6.5	72.48
Nanoemulgel 4	66850	6.2	61.35

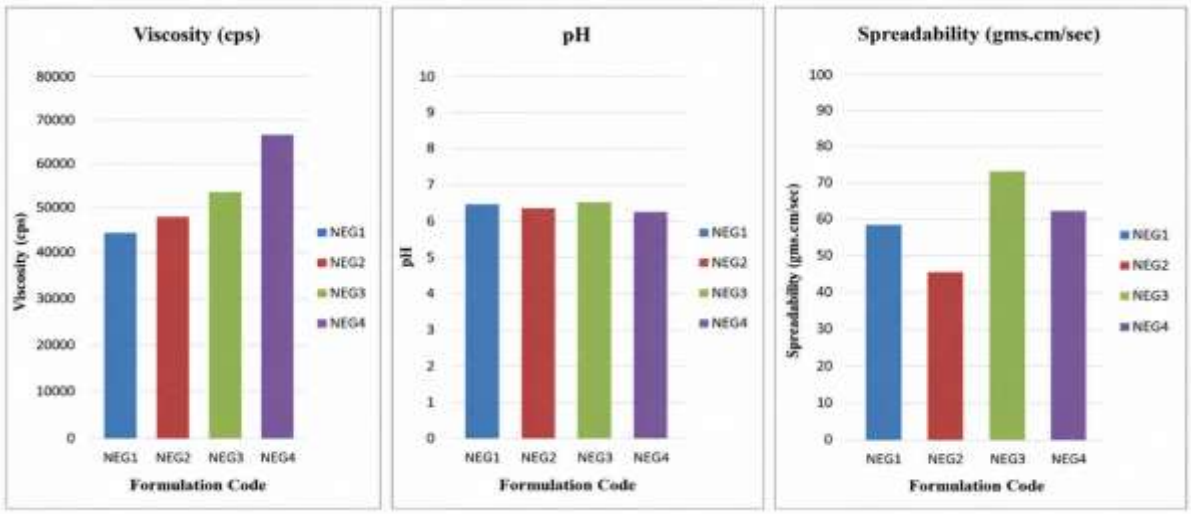

Figure 7.10: Viscosity, Spreadability &% Drug content

7.2.4.9. *In vitro* Diffusion Study:

All the prepared batches of β-sitosterol nanoemulgel exhibited good drug diffusion characteristics. The cumulative percentage of drug released from various batches of the nanoemulgels is shown in the table below. The maximum drug release was achieved by the batch NEG3 after 8 hrs i.e., 91.93%, which indicates that the diffusion property of the drug in this particular batch was higher.

Table 7.10: % *In-vitro* Drug Release of β-Sitosterol Nanoemulgel

Time (hr)	Nanoemulgel-1	Nanoemulgel-2	Nanoemulgel-3	Nanoemulgel-4
1	12.48	15.32	18.65	14.24

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2	20.36	24.48	30.52	22.68
3	29.15	35.26	42.73	33.40
4	38.82	47.68	55.84	45.92
5	49.20	58.34	67.15	56.73
6	58.74	69.25	78.86	66.42
7	66.58	77.84	86.15	74.28
8	72.46	84.62	91.93	80.36

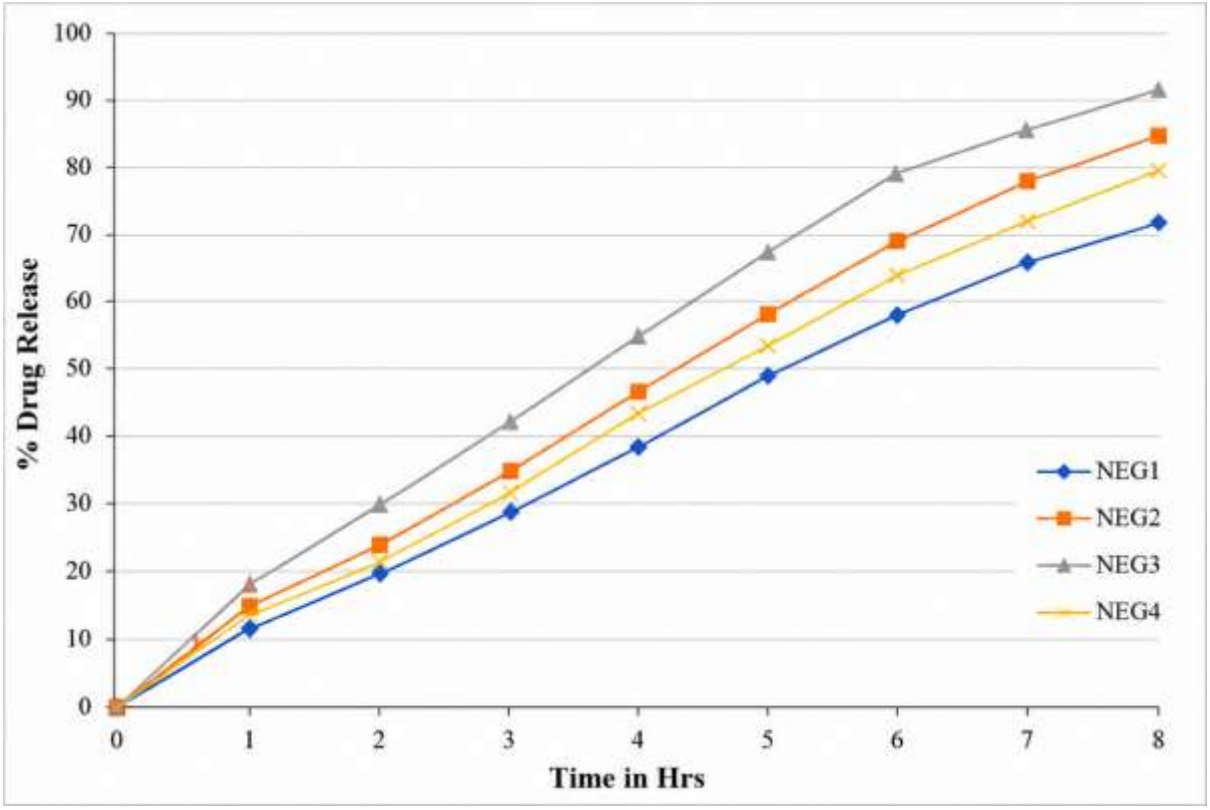

Figure 7.11: *In Vitro* Drug Diffusion

7.2.4.10. Stability studies

The stability of the finalized β-sitosterol nanoemulgel formulation (NEG-3) was studied under accelerated conditions of 40°C ± 2°C and relative humidity of 75% ± 5%. No significant alteration in the pH, viscosity, appearance, content, and *in vitro* drug diffusion profile was

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noticed during the entire period of three months. It has been concluded that the optimized β-sitosterol nanoemulgel formulation was stable under accelerated conditions

Table 7.11: Stability Study of β-Sitosterol Nanoemulgel

Parameters	Initial	1 Month	2 Month	3 Month
pH	6.5	NA	NA	NA
Viscosity	53680 cps	NA	NA	NA
Appearance	Transparent pale yellow	NA	NA	NA
In vitro Drug Diffusion (%)	91.93 ± 0.2	91.28 ± 0.3	89.76 ± 0.2	88.94 ± 0.1

NA=Not appearing any change

8. CONCLUSION

This current investigation was able to demonstrate the possible therapeutic utility of phytoconstituents derived from *Coccinia grandis* in managing patients with psoriatic arthritis using an integrated computational and formulation-based approach. Psoriatic arthritis is a type of inflammatory condition wherein the immune system is altered, leading to the destruction of joints and affecting the overall quality of life of the affected individuals. However, due to the adverse effects and expensive treatment regimens, as well as low efficacy rates and systemic toxicity, there should be an alternative treatment modality developed. As part of the initial steps undertaken in the computational stage, vital inflammatory targets associated with PsA, like IL-23, IL-17, and TNF-α, were identified and subjected to molecular docking tests. It turned out that the chosen phytoconstituents of *Coccinia grandis* have promising affinity and molecular interactions with the target proteins, making them probable inhibitors of inflammation in cases of Psoriatic Arthritis. More importantly, based on ADMET and drug-likeness analysis, β-sitosterol showed appropriate pharmacokinetics and safety profile. Based on the positive in silico results, β-sitosterol was chosen to be formulated into a topical drug carrier for therapeutic use. The obtained β-sitosterol-loaded cream showed adequate physicochemical properties like pH, viscosity, homogeneity, spreadability, washability, and drug loading. In addition, the β-sitosterol-loaded cream showed adequate stability and *in vitro* drug release kinetics, suggesting that it is effective for local delivery of β-sitosterol in the treatment of psoriatic arthritis. The

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designed delivery system might offer better efficacy at the target area without causing any systemic side effects, as oral or injectable drug formulations do.

In conclusion, this investigation has revealed that β-sitosterol derived from *Coccinia grandis* could have great therapeutic potential for the treatment of psoriatic arthritis. It can be concluded that the combination of computational drug discovery approaches and herbal formulations offers a scientific and economical technique for discovering new bioactive compounds from medicinal herbs. The formulated drug may be considered as a potential candidate for the management of Psoriatic Arthritis; however, further pharmacological

Acknowledgement

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Conflict of Interest

The authors declare no conflict of interest.

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