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Research Article

# ANTI-PSORIATIC POTENTIAL OF *FERNANDOA ADENOPHYLLA*: PHYTOCHEMICAL PROFILING, *IN-VIVO* EFFICACY AND *IN-SILICO* INSIGHTS

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## ABSTRACT

**Objective:** This study investigates the anti-psoriatic potential of *Fernandoa adenophylla* through phytochemical profiling, *in vivo* assessment using an imiquimod (IMQ)-induced psoriasis model in mice, and in silico molecular docking studies.

**Methods:** Methanolic extracts of *F. adenophylla* leaves and fruits were subjected to preliminary phytochemical and physicochemical analyses. In vivo efficacy was evaluated in IMQ-induced psoriasis-like mice through PASI scoring and histopathological examination. In silico docking of key phytoconstituents lapachone and peshawaraquinone was performed against cyclooxygenase-1 (COX-1, PDB ID: 4O1Z), followed by ADME and toxicity profiling.

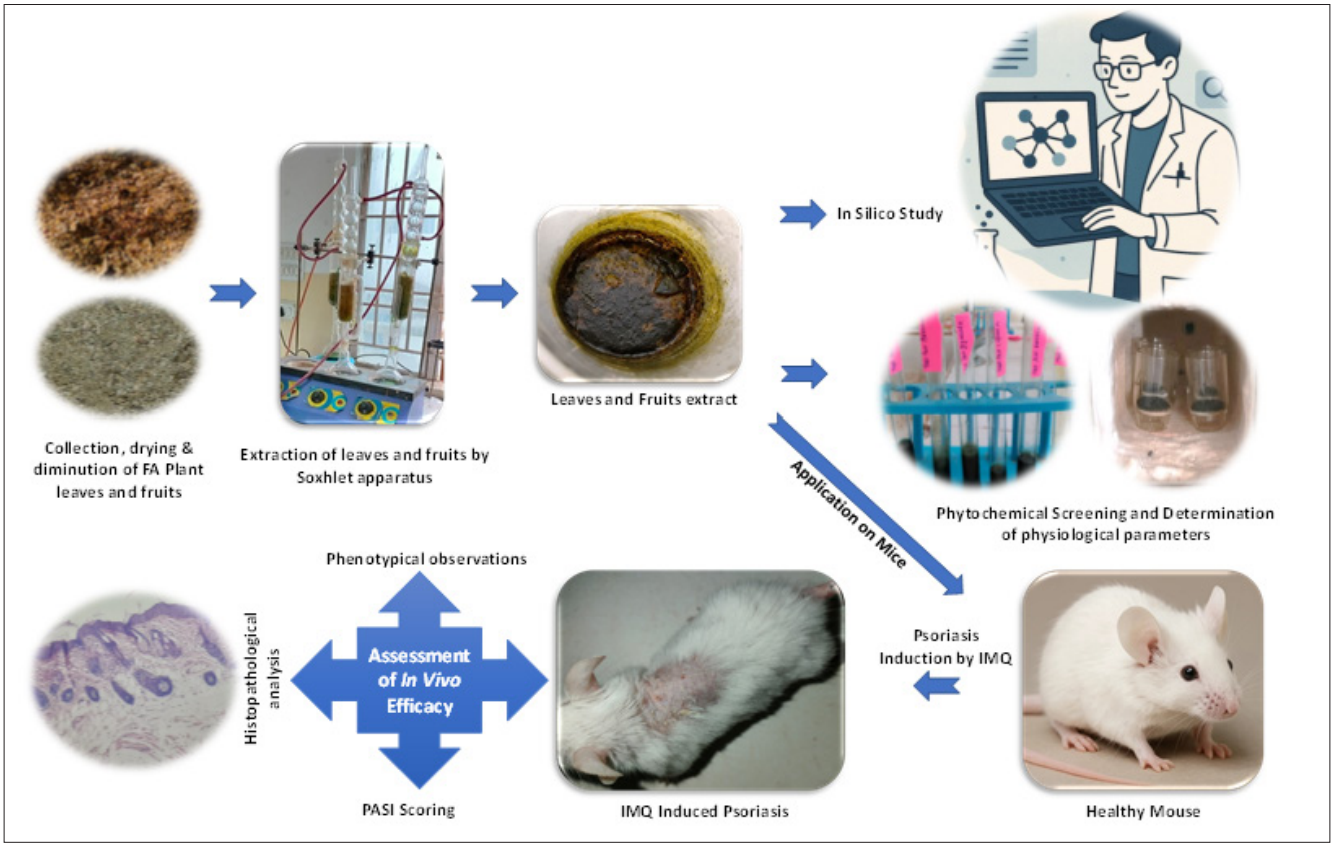
**Results:** Phytochemical screening revealed the presence of glycosides, alkaloids, tannins, saponins, steroids, and proteins. In vivo, both leaf and fruit extracts (particularly at 200 mg/kg) significantly reduced erythema, scaling, and epidermal thickening, comparable to ketoconazole (2%). Histological analysis confirmed normalized skin architecture in treated groups. Docking studies demonstrated strong binding affinities of lapachone and peshawaraquinone to COX-1, supported by favorable ADME properties and low predicted toxicity.

**Discussion:** The findings suggest that *F. adenophylla* exhibits significant anti-psoriatic effects, likely mediated through inhibition of inflammatory pathways involving COX-1. The therapeutic response aligns with the plant's bioactive constituents and traditional use in treating skin ailments.

**Conclusion:** *Fernandoa adenophylla* demonstrates potent anti-psoriatic activity with promising safety and pharmacokinetic profiles. This validates its potential as a phytotherapeutic candidate for psoriasis management and warrants further clinical investigation.

**KEYWORDS**: *Fernandoa adenophylla*, Psoriasis, Phytomedicine, Lapachone, Peshawaraquinone, Molecular Docking.

## Graphical Abstract




## Introduction

Psoriasis is a chronic, immune-mediated skin disorder characterized by epidermal hyperproliferation, aberrant keratinocyte differentiation, and sustained inflammation. Clinically, it manifests as erythematous plaques with silver-white scales, predominantly affecting extensor surfaces and the scalp. It is frequently associated with systemic comorbidities such as psoriatic arthritis, cardiovascular disease, and metabolic syndrome[1]. The disease pathogenesis involves a complex interplay between the innate and adaptive immune systems, with overactivation of Th1 and Th17 pathways contributing to inflammatory cascades. Key mediators include reactive oxygen species (ROS), phospholipase A2, and prostaglandins, particularly PGE2, which promote vasodilation, leukocyte infiltration, and keratinocyte proliferation[2,3]. Activated lesions of psoriasis are commonly identified by the infiltration of activated polymorphonuclear leukocytes into the epidermis. This infiltration triggers the excessive generation of reactive oxygen species, resulting in peroxidative harm to the skin's membrane. Additionally, the reactive oxygen species can stimulate Phospholipase A2, leading to an increased release of mediators associated with Arachidonic acid. The formation of prostaglandin E2 (PGE2) induces vasodilation in the blood vessels of the dermis, which subsequently promotes the penetration of leukocytes and stimulates the proliferation of keratinocyte cells[4]. Current pharmacological treatments for psoriasis include topical corticosteroids, vitamin D analogs, calcineurin inhibitors, systemic agents (e.g., methotrexate, cyclosporine), and biological therapies targeting cytokine pathways[5]. However, these approaches often suffer from limitations, including adverse effects, high cost, and resistance over time. Consequently, there is a growing interest in plant-derived therapies offering multi-targeted efficacy with fewer side effects[5-7]. The challenges and concerns surrounding allopathic pharmaceuticals persist in terms of their cost-effectiveness, availability, and the potential negative effects associated with their continued usage. In the present setting, herbal plants are demonstrating notable efficacy, thereby progressively establishing themselves as feasible alternatives to conventional pharmaceuticals for many ailments[8]. Numerous herbal plants have demonstrated potential as immunomodulators, exhibiting anti-inflammatory, antistress, and anticancer properties, as well as efficacy in treating diverse skin ailments[9]. The curative benefits of these botanical species and the imperative for empirical substantiation in traditional medicine have engendered heightened scholarly attention in this domain[10]. The current study aims to assess the anti-psoriatic effectiveness of the medicinal plant *Fernandoa adenophylla*[11].

*Fernandoa adenophylla (Haplophragma adenophyllum),* belonging to the Bignoniaceae family, is traditionally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used for treating skin conditions, haemorrhoids, and other inflammatory disorders in South and Southeast Asia[12]. Previous phytochemical investigations report its richness in bioactive compounds such as lapachone, peshawaraquinone, and lapachol - quinone derivatives with known anti-inflammatory, antioxidant, and antimicrobial activities[10,13–17]. Given this traditional and pharmacological relevance, the present study evaluates the anti-psoriatic potential of *F. adenophylla* through a multifaceted approach, including phytochemical profiling, pharmacognostic assessments, in vivo efficacy in an imiquimod-induced mouse model, and in silico molecular docking studies targeting cyclooxygenase-1 (COX-1).

## Material and Method

### Chemicals and Reagents

All solvents and reagents used were of analytical grade. Ketoconazole cream (2%) was procured from Aurochem Laboratories Pvt. Ltd., and imiquimod (IMQ) cream (5%) was obtained from Glenmark Pharmaceuticals. All chemicals required for phytochemical testing were obtained from the NIMS Institute of Pharmacy.

### Plant Collection and Authentication

Leaves and fruits of *Fernandoa adenophylla* were collected from the Geological Survey of India (NCEGR), Faridabad, and authenticated by the Department of Pharmacognosy, NIMS University, Jaipur. Plant materials were shade-dried, pulverized, and stored in airtight containers until further use.

### Extraction and Isolation

Two hundred grams of powdered leaves and fruits were subjected to Soxhlet extraction using methanol for 72 hours. The extracts were filtered and concentrated under reduced pressure using a rotary evaporator to yield crude methanolic extracts[18].

### Preliminary Phytochemical Screening

Standard qualitative methods were used to detect major phytochemical groups, including carbohydrates (Fehling's test), proteins (Biuret and Millon's tests), glycosides (Keller–Killiani test), saponins (foam test), flavonoids (sulfuric acid test), tannins (FeCl3 test), alkaloids (Dragendorff's and Hager's tests), and steroids (Salkowski test)[18].

### Physicochemical Evaluation

Physicochemical parameters of powdered plant material were determined as per WHO guidelines, including[19] circumscribed, scaly, and erythematous plaques that can cover large skin areas. While conventional treatments such as topical corticosteroids and systemic medications are commonly prescribed, the interest in natural remedies for psoriasis has grown due to concerns about potential side effects and the desire for alternative treatment options. Rosa × damascena Mill. is rich in bioactive compounds that possess anti-inflammatory, antioxidant, and antimicrobial properties; these properties make Rosa × damascena Mill. a promising candidate for the management of skin disorders such as psoriasis. In our previous studies, we successfully formulated and tested different topical preparations containing Rosa × damascena Mill. In this study, we investigated the correlation between the Psoriasis Area and Severity Index (PASI:

#### *Loss on drying*

Samples (2 g) were dried at 105 °C until a constant weight was achieved.

#### *Ash value*

Total ash, water-soluble ash, and acid-insoluble ash were evaluated using standard procedures[18,20].

#### *Extractive value determination*

Water-soluble and alcohol-soluble extractive values were assessed via maceration followed by evaporation[18].

## Molecular Docking Studies

The 3D structure of ovine COX-1 (PDB ID: 4O1Z) was retrieved from the RCSB Protein Data Bank. Protein preparation involved removal of heteroatoms, addition of hydrogen atoms, and energy minimization using a CHARMM force field. Ligand structures were drawn in ChemDraw 15.1 and optimized. Docking simulations were performed using LibDock (Accelrys Discovery Studio Version 2.0 software). Docking scores and key interactions were recorded[21–23].

### Homology Modeling and Structure Validation

The geometry and quality of the protein model were validated using PROCHECK, generating Ramachandran plots and main-chain parameter statistics.

### ADME and Toxicity Profiling

ADME properties (like molecular weight, hydrogen bond acceptors/donors, log P) of alpha-lapachone and peshawaraquinone were predicted using computational tools. Toxicity endpoints (hepatotoxicity, mutagenicity, carcinogenicity, immunotoxicity, cytotoxicity) were evaluated using the ProTox-II server.

## Animal Studies

### Animal Handling and Ethical Approval

Healthy albino mice (8–10 weeks, 25–35 g) were maintained under controlled conditions at NIMS Institute of Pharmacy. All protocols were approved by the Institutional Animal Ethics Committee (IAEC) under protocol no. 1302/PO/RE/S/09/CPCSEA. Throughout the whole experimental duration, the animals were provided with a well-balanced commercial diet and unrestricted access to water [24].

### Induction of Psoriasis-like Dermatitis

The care and procedures implemented throughout the animal experiments adhered to the national guidelines for the

care and utilization of laboratory animals. A cohort of 30 albino mice in good health underwent dorsal hair removal. The mice were subjected to a daily dose of 62.5mg of 5% imiquimod cream applied to the shaved dorsal skin for a period of seven consecutive days[24–26].

### Treatment Groups

Following the induction of psoriasis, the mice were subjected to random allocation into seven distinct groups and subsequently administered treatments[27,28] immune-mediated inflammatory skin disease, and the inflammatory response plays an important role in its development and progression. Psoriasis can appear at any age and occurs around the world. The pathogenesis of psoriasis has not been fully elucidated, and there is currently no effective treatment method in clinical practice. Broussonetia papyrifera is a traditional Chinese medicine that exhibited a significant therapeutic effect on psoriasis in our previous study due to its remarkable anti-inflammatory and anti-oxidant properties. However, its mechanism of action in treating psoriasis is still unclear. The purpose of this study is to evaluate the anti-psoriasis effect of the B. papyrifera leaves extract (PLE as outlined in the accompanying Table 1. The test substance was freshly prepared before administration to the mice, and a standard reference, namely marketed ketoconazole, was used (Figure 1 (a)(b)).

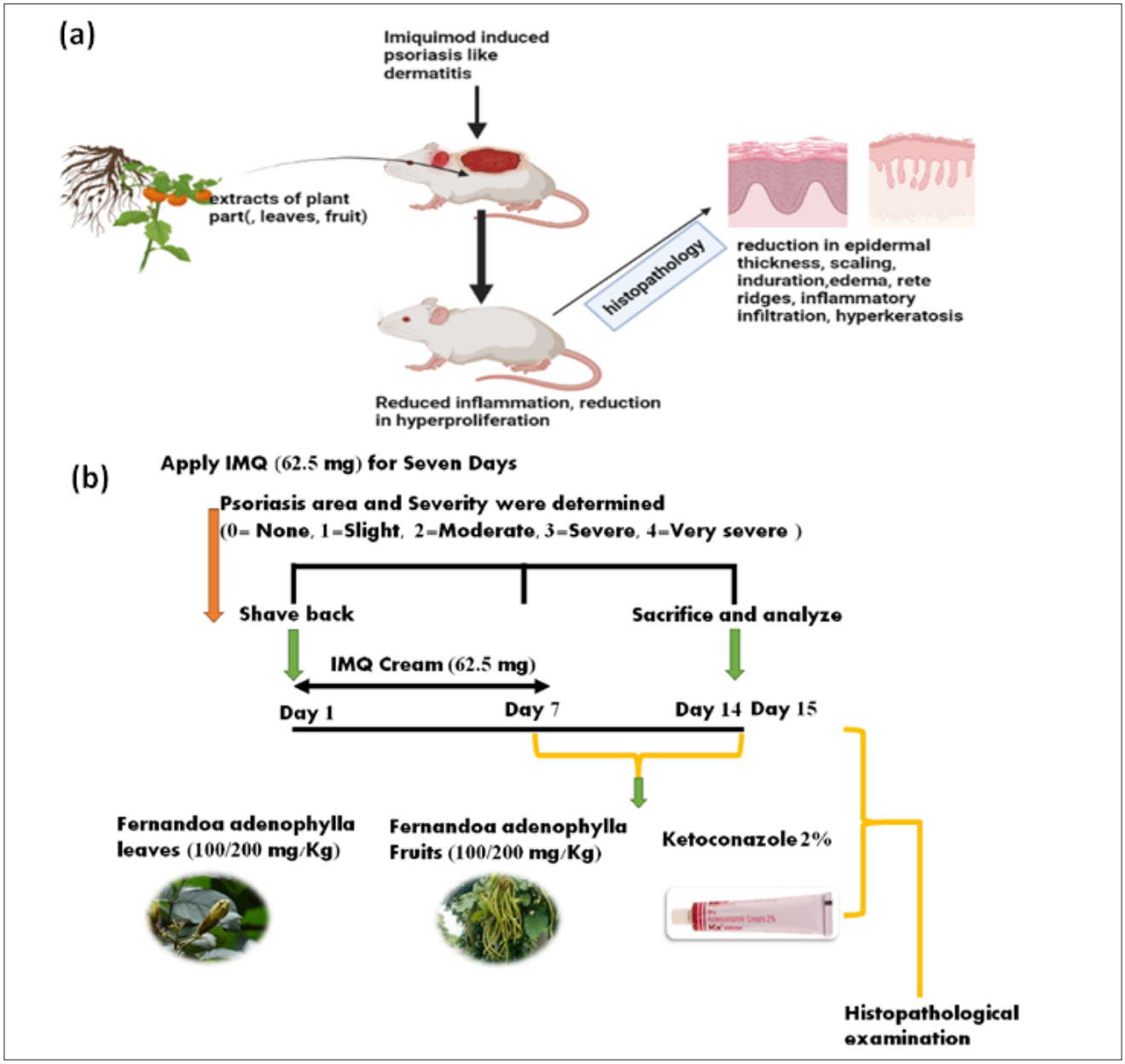


**Figure 1(a): Imiquimod-induced model for the treatment of psoriasis by plant parts (Leafs and Fruits)**

**Figure 1(b): Experimental procedure to induce psoriasis-like dermatitis. IMQ, Imiquimod; FA, Fernandoa adenophylla, KTZ, ketoconazole**


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**Table 1: Group Description**

| S. No. | GROUPS DESCRIPTION | Quantity |
|---|---|---|
| 1. | Normal control (Vaseline) | **N=4** |
| 2. | Toxic control (Imiquimod 5% w/w only) | **N=4** |
| 3. | Imiquimod + Ketoconazole cream (2% w/w) | **N=4** |
| 4. | Imiquimod + Lower dose of leave extract (100mg/kg) | **N=4** |
| 5. | Imiquimod + Higher dose of leave extract) (200mg/kg) | **N=4** |
| 6. | Imiquimod + Lower dose of fruit extract (100mg/kg) | **N=4** |
| 7. | Imiquimod + Higher dose of fruit extract (200mg/kg) | **N=4** |
| **Total Animal** | | **28** |

### PASI Scoring

An objective scoring system was devised to assess the severity of inflammation of the dorsal skin. Severity of erythema, scaling, and skin thickness was scored on a scale of 0–4 based on the modified Psoriasis Area Severity Index (PASI)[29,30].

### Sample Collection

At the conclusion of the experiment, mice belonging to groups I through VII were euthanized via intraperitoneal injection of pentobarbital at a dosage range of 50-90 mg/kg. The utilisation of pentobarbital in this study was based on its established profile regarding the duration of sleep and the loss of righting reflex after its administration. Groups II to VII of mice were subjected to IMQ treatment for a duration of 7 days, followed by administration of plant extract and ketoconazole treatment from day 7 to day 14. Subsequently, on the fifteenth day, the subjects were subjected to sacrifice within the confines of the laboratory. Skin tissue measuring approximately 1 cm2 from the central dorsal region was extracted from all experimental groups for histological examination[31].

### Histopathological Evaluation

The tissue samples that were chosen for analysis were subjected to fixation in a solution of 10% neutral-buffered formalin. Following this, the samples were processed and embedded in paraffin blocks. The specimens were sectioned to a thickness of 4 µm using a rotary microtome and subsequently subjected to haematoxylin and eosin (H&E) staining. The samples were then examined under a microscope equipped with a digital camera system[27,32].

### Statistical Analysis

TThe study employed a one-way analysis of variance (one-way ANOVA) to examine the variations between treatment groups. Subsequently, Fisher's least significant difference (LSD) test was conducted as a post hoc analysis. The statistical analysis was performed using SPSS for Windows (version 20.0). Statistical significance was determined at a level of $P < 0.05$. The experiments were conducted in triplicate with a minimum of three replicates. The values are presented in the form of mean ± standard deviation (SD)[33].

## Results

### Phytochemical Composition

Preliminary phytochemical screening of *Fernandoa adenophylla* leaves revealed the presence of carbohydrates, glycosides, saponins, tannins, alkaloids, steroids, and proteins. Flavonoids were absent in leaf extracts but present in the fruit extracts. Both parts demonstrated a rich diversity of secondary metabolites (Table 2), suggesting potential pharmacological relevance.

### Physicochemical Parameters

The physicochemical evaluation indicated that total ash content was 7.0% for leaves and 8.0% for fruits, with water-soluble ash values of 9.3% and 9.6%, respectively. Acid-insoluble ash was slightly higher in fruits (11.0%) than in leaves (8.0%). Loss on drying was minimal, 0.5% for leaves and 1.0% for fruits, indicating low moisture content. Water-soluble extractive values were 6.8% (leaves) and 6.2% (fruits), confirming satisfactory extractability of active constituents[34] (Table 3).

### Molecular Docking Analysis

In the present study, 4O1Z showed a MolProbity score of 1.35 which determines the correctness and quality of protein structure. The φ and ψ scores of the residues are plotted on the background. In 4O1Z, 89.5% of the residues were lying in the Ramachandran favored region and 10.5% of the residues lying in additional allowed regions. The 3D geometry of the protein model was determined by the PROCHECK web tool, which calculate the Ramachandran plot and generated results for residues showing regions with different colors, like red (favored), yellow (additionally allowed), pale yellow (generally allowed), and white colored areas (disallowed) shown in Figure 2 (a). In 4O1Z, a total of 1106 residues were found, out of which 841 (89.5%) of the residues lied in the most favored region [A,B,L], 99 (10.5%) residues in additional allowed regions (a,b,l,p). Moreover, none of the residues were found in generously allowed regions and disallowed regions. Additionally, 940

(100%), non-glycine and non-proline residues were found, and 2 residues were the end residues (excluding glycine and proline), number of glycine residues (shown as triangles) were 84 and proline residues were 80 respectively (Figure-2 **(a)**). The six graphs on the main-chain parameters plot show hoe the structure (represented by the solid square) compares with well-refined structures at a similar resolution (Figure-2 (b)). The dark band in each graph represents the results from the well-refined structures; the central line is a least-squares fit to the mean trend as a function of resolution, while the width of the band on the either side of it corresponds to a variation of one standard deviation about the mean. In some cases, the trend is depended on the resolution, and in other cases, it is not.

**Table 2: Phytochemical identification of *Fernandoa adenophylla* leaves and fruit**

| **Phytochemical identification of *Fernandoa adenophylla* leaves** | | | |
|---|---|---|---|
| **Phytochemicals** | **Test** | **Observation** | **Inference** |
| Carbohydrates | Fehling's test | Brick red ppt | Carbohydrates present |
| Flavonoid | Sulfuric acid test | Absence of orange to red color | Flavonoid absent |
| Glycoside | Keller-killani test | Reddish brown color appears | Glycoside present |
| Saponin | Foam test | Thick persistent foam observed | Saponin present |
| Tannin | 5% FeCl3 test | Deep blue -black color | Tannin present |
| Alkaloid | Dragendorff's test | Orange -brown ppt | Alkaloid present |
| Steroid<br>Salkowski reaction test | | Chloroform layer appear red and acid layer shows greenish yellow color | Steroid present |
| Protein | Million's test for protein | White ppt | Protein present |
| **Phytochemical identification of *Fernandoa adenophylla* Fruit** | | | |
| Carbohydrates | Fehling's test | Brick red ppt | Carbohydrates present |
| Flavonoid | Sulfuric acid test | orange to red color | Flavonoid present |
| Glycosides | Keller-killani test | Reddish brown color appears | Glycoside present |
| Saponin | Foam test | Thick persistent foam observed | Saponin present |
| Tannin | 5% FeCl3 test | Deep blue -black color | Tannin present |
| Alkaloid | Dragendorff's test | Orange -brown ppt | Alkaloid present |
| Steroid | Salkowski reaction | The chloroform layer appears red, and the acid layer shows a greenish-yellow colour | Steroid present |
| Protein | Million's test | White ppt | Protein present |

**Table 3: Physiochemical parameters of *Fernandoa adenophylla***

| **Physiochemical parameters of *Fernandoa adenophylla* leaves** | | |
|---|---|---|
| **S. No.** | **Parameters** | **Value (w/w %)** |
| 1. | Total ash | 7 |
| 2. | Water soluble ash | 9.3 |
| 3. | Acid soluble ash | 8 |
| 4. | Loss on drying | 0.5 |
| 5. | Water soluble extractive value | 6.8 |
| **Physiochemical parameters of *Fernandoa adenophylla* fruits** | | |
| 6. | Total ash | 8 |
| 7. | Water soluble ash | 9.6 |
| 8. | Acid soluble ash | 11 |
| 9. | Loss on drying | 1 |
| 10. | Water soluble extractive value | 6.2 |


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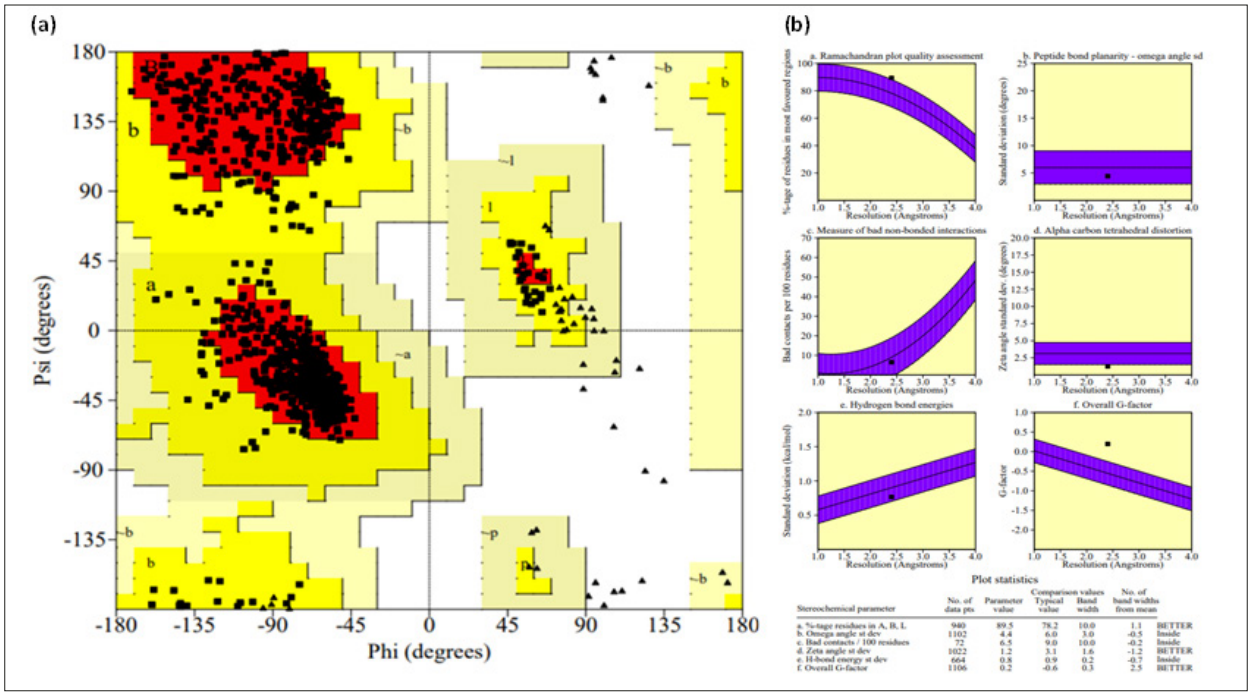


**Figure 2(a): Ramachandran plot of 4O1Z: PROCHECK residue analysis with plot statistics**
**Figure 2(b): Plot Statistics of the main chain parameters of 4O1Z protein**

The quality of Ramachandran plot is shown in Figure 2 (b), and this feature measures the protein residues percentage that lies in the favored or core region. Our protein model showed that 89.5% of residues are present in the favored region. Figure 2 (b) represents the planarity of the peptide bond that is measured by determining the standard deviation of the protein structure's omega torsion angles. In our study, an omega standard deviation value of 4.4 was found which is considered better for a protein structure. The bad non-bonded interactions measure the number of bad contacts per 100 residues and parameter value of 6.5 was found. Further study shows that the alpha carbon tetrahedral distortion that gives a measure of the standard deviation of zeta torsion angle was found to be 1.2. The main chain hydrogen bond energy feature determines the hydrogen bond standard deviation for the hydrogen bonds of the main chain and the parameter value of 0.8 was found. Moreover, the G-factor that measures the overall normality of the protein structure was found to be 0.2 (Figure 2 (b)).

**Binding interactions between the identified compounds and Ovine Cyclooxygenase-1 complex with meloxicam Protein (4o1z)**

To examine the binding interactions with the 4o1z receptor, molecular docking was performed using the identified compounds from the leaves and fruits extract of *Fernandoa Adenophyllum* viz. Lapachone and Peshawaraquinone. Binding affinity (docking scores) and hydrogen bonding catalytic residue for the chosen compounds against Ovine Cyclooxygenase-1 complex with meloxicam Protein, PDB identification: 4o1z) are presented in Table 4[35]. These outcomes revealed that the compounds Lapachone and Peshawaraquinone were observed to be the most active moieties. The Lapachone was docked in the active site of 4o1z and the LibDock score was observed to be 135.399 (Table 4).

**Table 4: Docking Scores, amino acid residues and H- bond distances of the identified compounds**

| Compound | Docking Score | Amino Acid Residues | H-Bond Distance |
|---|---|---|---|
| Lapachone | -8.6 | O-Arg322<br>H-Asp233<br>H-His231<br>H-His307<br>H-Asn205 | 3.323479<br>2.39477<br>2.34403<br>2.86729<br>2.12754 |
| Peshawaraquinone | -7.7 | H-Ser318 | 2.49226 |

The binding modes of lapachone demonstrated conventional hydrogen bond with pi- donor and carbon hydrogen bonds in addition to three hydrophobic pi- alkyl interactions (Figure 3 (a)). The 3- hydroxyl group and a carbonyl group of 3- carboxylic acid moiety present in the 1- indanone ring of Lapachone showed strong hydrogen bond with His 386 which reportedly has been playing a very crucial role in the binding of natural ligands as well as 4O1Z inhibitors[36]. A Carbon hydrogen bond formation was apparent between hydrogen of His 388 and oxygen of the 3- carboxyl group present in the structure of lapachone. On the other hand, hydrophobic interactions were observed with Phe 210, His 207, and Ala 202. The earlier reports have also identified the importance of hydrophobic interaction[36] of potent 4o1z inhibitors, due to the presence of 2- isopentenyl group that provides prominent hydrophobic environment in the binding site. Moreover, another important Pi- donor hydrogen bond interaction was observed between 1- carbonyl oxygen of Indanone moiety and hydrogen of Thr 206, and Trp 387 was also viewed interacted with an indanone ring present in the structure of Lapachone (Figure 3 (a)).

The binding approaches of Peshawaraquinone exhibited one hydrogen bond, one van der Waals and five hydrophobic interactions in addition to one pi- donor hydrogen bond and pi- sulphur interaction (Figure 3 (b)). Peshawaraquinone was docked in the active site of 4o1z and the LibDock score was observed to be 133.299 (Table 4). The 2- hydroxyl group of naphthoquinone moiety of Peshawaraquinone formed the strong hydrogen bond interaction with Thr 206 binding site. Additionally, its naphthaquinone ring also showed van der Waals interaction with the -NH moiety of Trp 387, with a strong Pi-donor hydrogen bonding with Gln 203 amino acid residue. On the other hand, hydrophobic pi- alkyl interactions were observed with Phe 210, His 386, His 207, Leu 390 and Ala 199 on active sites of 4o1z receptor. Moreover, additional essential Pi- Sulfur interaction was observed between sulphur of Met 391 and naphthoquinone ring of Peshawaraquinone. Finally, the results of molecular docking study clearly show that the Lapachone and Peshawaraquinone (Figure 3 (a) and (b)) possesses the essential structural features required to interact with the active site amino acids and this makes these compounds suitable candidate for the inhibition of the 4o1z receptor.

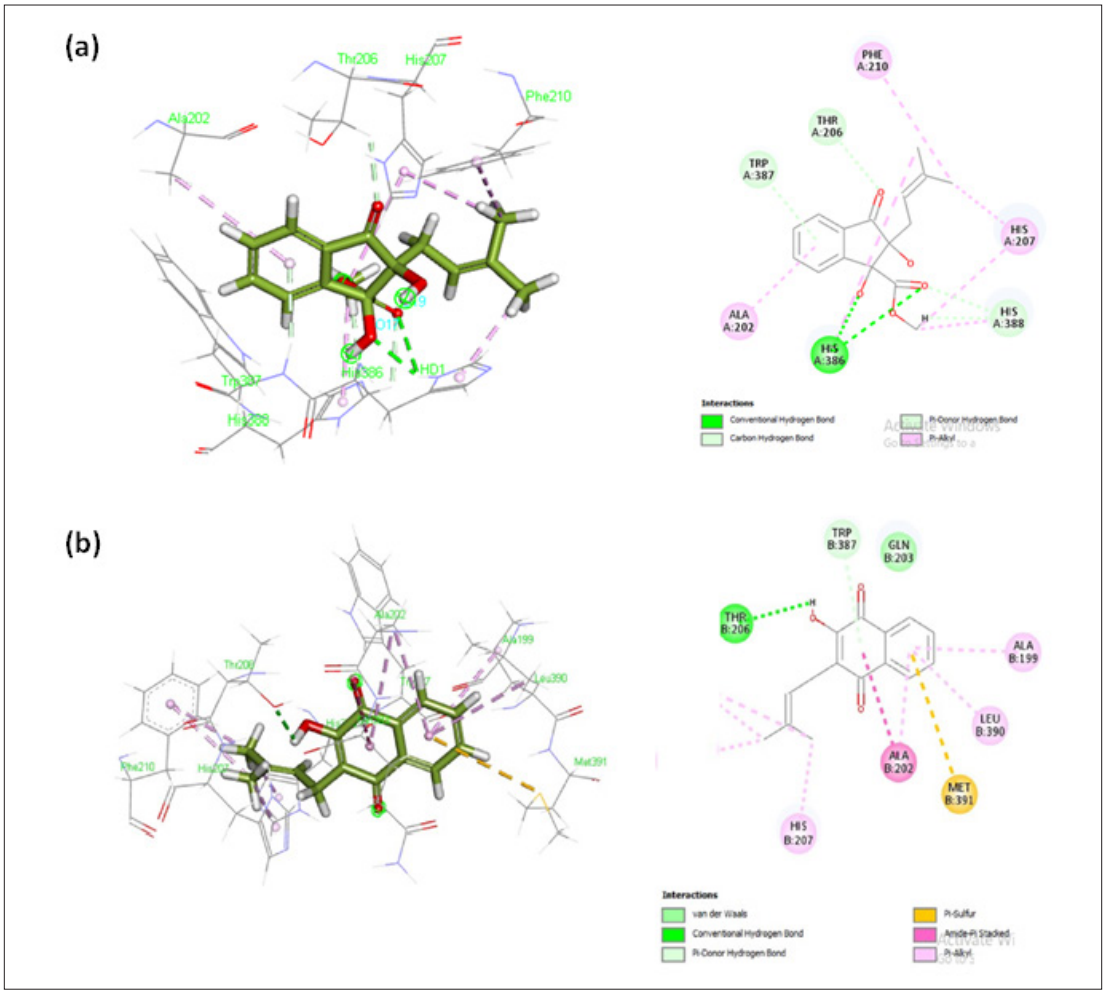


**Figure 3(a): Docking analysis of Compound Lapachone**
**Figure 3(b): Docking analysis of Compound Peshawaraquinone**


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**Table 5: ADME properties of Alpha-Lapachone & peshawaraquinone**

| Compound | ADME Weight | ADME H-Bond Acceptor | ADME H-Bond Donor | ADME LOG P | ADME Violation |
|---|---|---|---|---|---|
| Alpha-lapachone | 290.34 | 5 | 2 | 1.267 | 0 |
| Peshawaraquinone | 242.29 | 3 | 1 | 1.5013 | 0 |

**Table 6 Toxicity Studies**

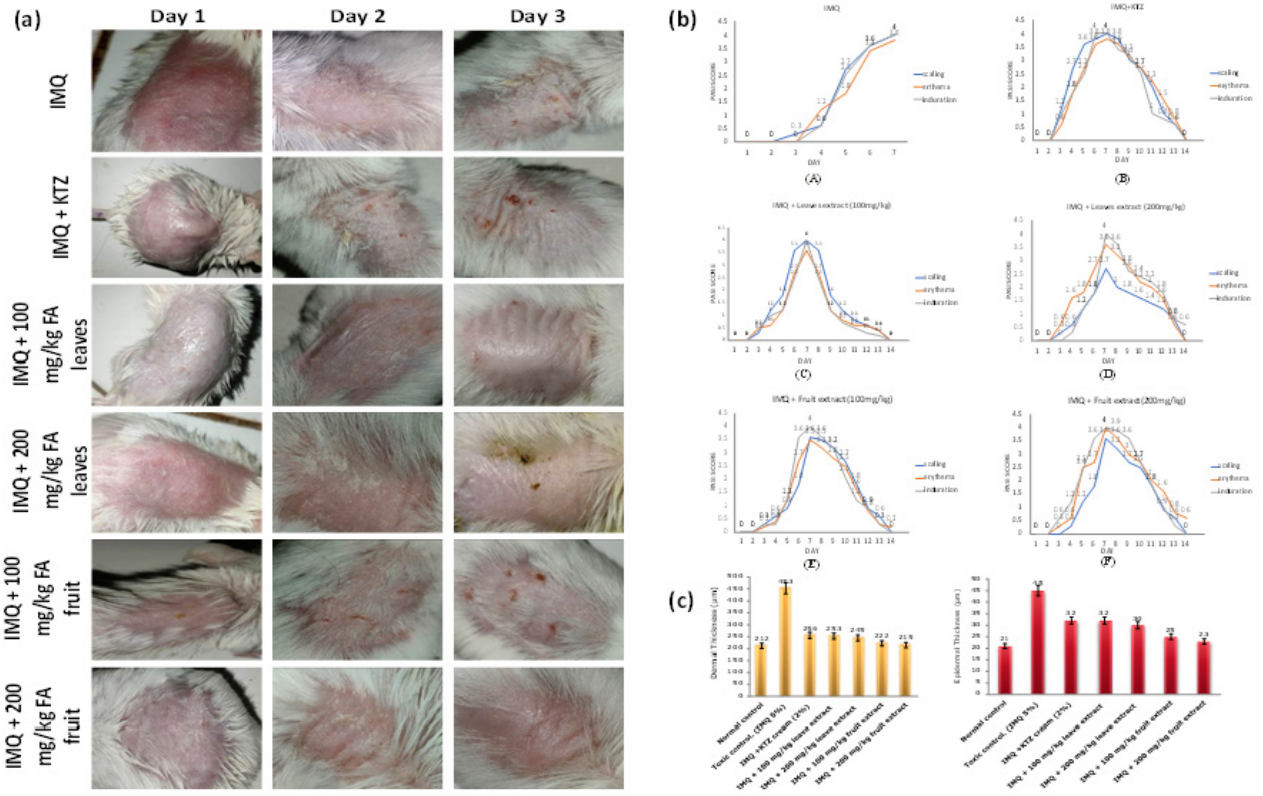
| Compound | Hepatotoxicity | Carcinogenicity | Mutagenicity | Immunotoxicity | Cytotoxicity |
|---|---|---|---|---|---|
| Alpha-lapachone | 0.66 | 0.53 | 0.68 | 0.98 | 0.72 |
| Peshawaraquinone | 0.64 | 0.62 | 0.79 | 0.71 | 0.51 |

### *ADME and Toxicity Profiling*

Both compounds complied with drug-likeness rules, displaying favorable ADME profiles including appropriate molecular weights, log P values, and hydrogen bond acceptor/donor counts. ProTox-II predictions indicated low toxicity risks, with no violations related to hepatotoxicity, mutagenicity, or carcinogenicity (Tables 5 and 6).

### *In Vivo* Efficacy in IMQ-Induced Psoriasis-like Model

Application of imiquimod induced erythema, scaling, and thickening of the dorsal skin, validating the psoriasis model. No pathological changes were observed in the control group treated with Vaseline. Following treatment, a significant reduction in PASI scores was observed across all extract-treated groups. Leaf and fruit extracts of F. adenophylla at 200 mg/kg exhibited efficacy comparable to ketoconazole (2%), showing marked improvements in erythema, scaling, and epidermal thickening (Figure 4 (b)). The therapeutic effects were dose-dependent. The Figure 4 (b) illustrate the independent PASI scores, which indicate a gradual escalation in the degree of inflammation after the administration of IMQ, from day 1 to 7, prior to the commencement of either ketoconazole or leaves/fruit extract of *Fernandoa adenophylla* intervention. The PASI score exhibited its maximum intensity on the seventh-day post-IMQ treatment, thereby signifying the successful induction of psoriasis [28,37,38].



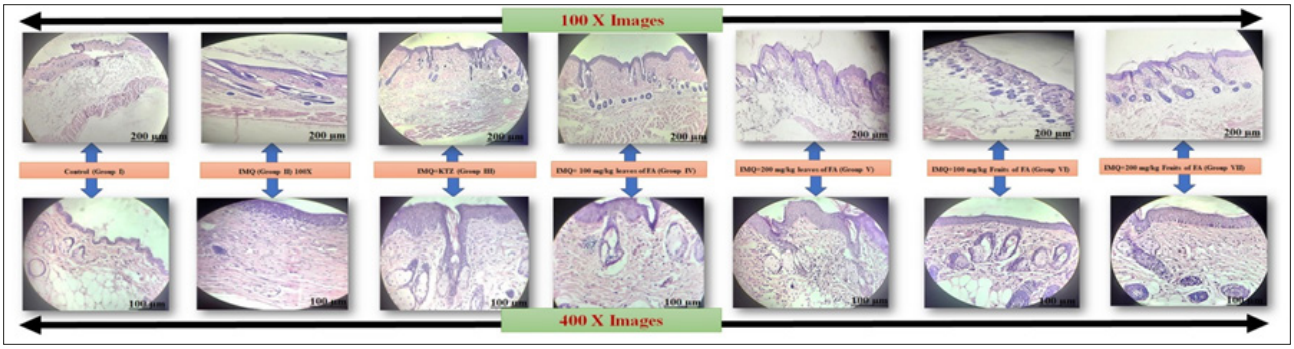



**Figure 4 (a): Phenotypical presentation of dorsal skin of the seven-dermatitis group; group II (IMQ), group III (IMQ + Ketoconazole), group IV (FA leaves 100mg/kg+IMQ), group V (FA leaves 200mg/kg+IMQ), group VI (FA fruit 100mg/kg+IMQ), group VII (FA fruit+ 200mg/kg+IMQ)**

**Figure 4 (b): Graphical presentation of the effect of the Fernandoa adenophylla treatment on the dorsal skin of IMQ-induced psoriasis dermatitis. Group A (IMQ); GROUP B (IMQ+KTZ 2%); GROUP C (IMQ+ FA leaves 100mg/kg); group D (IMQ+ FA leaves 200mg/kg); Group E (IMQ+ FA fruit 100mg/kg); Group F (IMQ+ FA fruit 200mg/kg). PASI score showing intensity of erythema, scaling, induration of the control and treated mice dorsal skin on a 0–5-point scale. Statistically significant at P<0.001 compared with all other groups. KTZ, Ketoconzole; IMQ, Imiquimod; FA, Fernandoa adenophylla**

**Figure 4 (c): Dermal and epidermal thickness of dorsal skin.**

**Figure 4 (d): Histological examination of the seven different groups, stained with haematoxylin and eosin.**

## Phenotypical Observations

The study of *Fernandoa Adenophylla* IMQ-induced inflammation reveals the manifestation of erythema, thickening, and scaling within a span of 2 to 3 days after the initial IMQ application. The highest degree of inflammatory severity is observed on days 7 and 8. The intensity of the psoriasis-like condition was observed to have exhibited a steady increase from day 1 to day 16[39]. The study reveals a notable reduction in psoriasis-like symptoms from day 8 onwards, following the second treatment cycle with either ketoconazole (group III) or *Fernandoa adenophylla* extract (group IV-VII) (Figure 4 (a)). The symptoms exhibit a consistent decrease in severity until the conclusion of the ketoconazole and *Fernandoa Adenophylla* therapeutic regimen on day 14. The (Figure 4 (b)) illustrate the PASI scores of each group from day 1 to day 14. In comparison to the IMQ-induced group, all groups treated with extract exhibited a notable suppressive impact on psoriasis-like dermatitis induced by IMQ. The study findings indicate that the administration of *Fernandoa adenophylla* at doses of 100 and 200 mg/kg body weight in mice resulted in a reduction of the inflammatory symptoms of psoriasis area severity index (PASI) in a dose-dependent manner. The observed decrease in PASI scores among the group treated with ketoconazole was found to be like that of the group treated with 200mg/kg of *fernandoa adenophylla* extract[40,41].

Control dorsal ski tissue section shows normal epidermis, dermis, sebaceous glands, and hair follicles. (I) Dorsal skin tissue section of IMQ treated mice shows flaky crust, acanthosis, and hyperkeratosis of the epidermis. Abundant inflammatory and elongated rete ridges were also shown with the IMQ treated group.(II) After treatment for 7 days, ketoconzole treated group shows decreased in the inflammatory infiltration of the epidermis.(III) *Fernandoa adenophylla* (leaves) 100 mg/kg shows slightly reduced inflammatory infiltrates. (IV) *Fernandoa adenophylla* (leaves) 200 mg/kg group shows significant decrease in the thickened epidermis, hyperplasia and inflammatory infiltration. (V) *Fernandoa adenophylla* (fruit) 100/200mg/kg showed the maximum efficacy of the treatment with the recovered having normal epidermis, dermis (VII, VIII).

## Histopathological Analysis

Histopathological analysis supported the examination of H&E-stained sections obtained from the dorsal skin treated with IMQ demonstrated consistency with the phenotypical observations and PASI score outcomes. The group that received imiquimod treatment had a notable rise in acanthosis, hyperkeratosis of the epidermis, and inflammatory infiltration in the dorsal skin region. In contrast, the dorsal skin portion of the control group had normal characteristics in terms of both epidermal and dermal areas (Figure 4 (c)). It is noteworthy that the mice treated with ketoconazole and *Fernandoa adenophylla* exhibited a significant reduction in epidermal thickness when compared to the mice treated with IMQ. The mice that received a dosage of 200 mg/kg of leaf extract exhibited a comparable effect to the group treated with ketoconazole. In both cases, there was total restoration from the IMQ-induced hyperplasia of the epidermis, accompanied by a

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slight inflammatory response. The mice in groups VI and VII, which were given fruit extract doses of 100 and 200 mg/mg, respectively, had significant recovery effects in response to IMQ-induced psoriasis (Figure 4 (d)). Nevertheless, it was observed that the group III mice, which were administered a dosage of 100 mg/kg of leaves extract, had the least significant antipsoriatic effects in comparison to the other experimental groups [42,43].

## Proposed Mechanism of Action

Based on the phytochemical profile, *in vivo* efficacy, and *in silico* findings, the anti-psoriatic activity of *Fernandoa adenophylla* can be attributed to multiple, complementary mechanisms. Lapachone and peshawaraquinone, the principal bioactive compounds identified, demonstrated strong binding affinity to the cyclooxygenase-1 (COX-1) active site in molecular docking studies, indicating their potential to attenuate prostaglandin-mediated inflammatory responses. In psoriasis, activation of the Th1/Th17 immune axis leads to elevated pro-inflammatory cytokines such as TNF-α, IL-6, IL-17, and IL-23, which drive keratinocyte hyperproliferation and epidermal thickening (Figure 5)[44]. The observed reduction in PASI scores and histological restoration in treated groups suggests that *F. adenophylla* extracts likely exert their effects by suppressing pro-inflammatory cytokine production via Potential inhibition of NF-κB and JAK/STAT signalling, thereby reducing transcription of TNF-α, IL-6, IL-17, and IL-23, Modulating oxidative stress due to the presence of phenolic and quinone-based compounds may neutralise reactive oxygen species (ROS), preventing activation of phospholipase $A_2$ and arachidonic acid pathways and restoring epidermal homeostasis via downregulation of keratinocyte proliferation and normalization of epidermal differentiation, evidenced by reduced acanthosis and hyperkeratosis in histology[45].

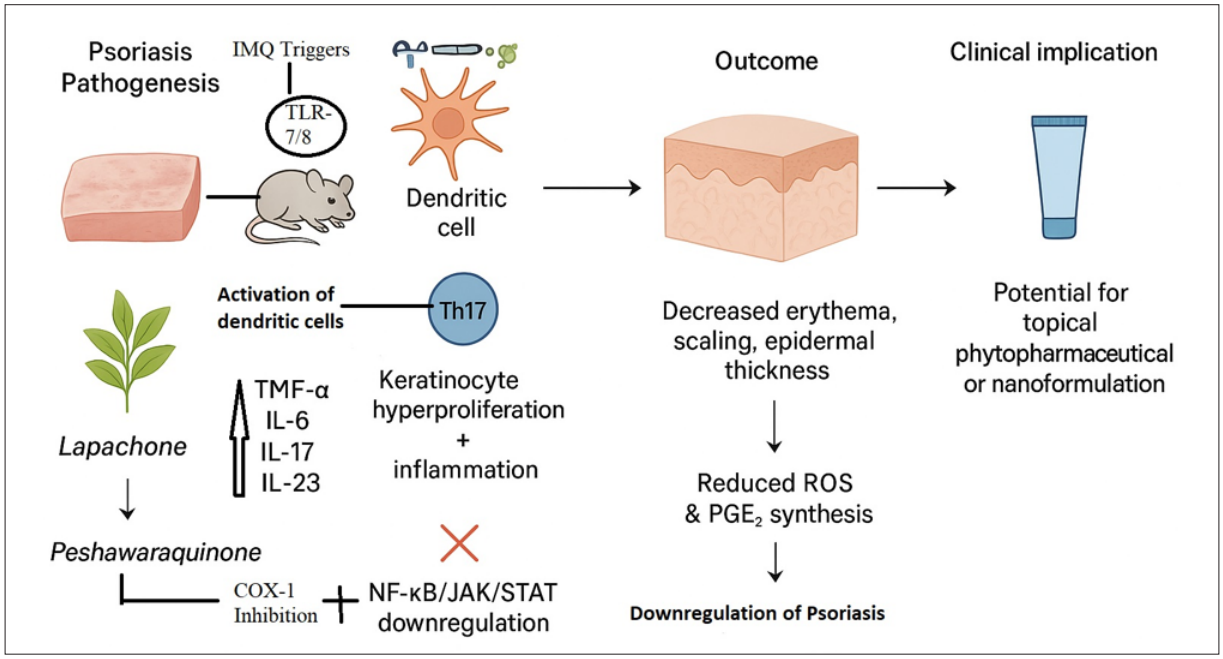


**Figure 5: Proposed mechanism of antipsoriatic action of Fernandoa Adenophylla**

## Discussion

Psoriasis is a persistent and recurring medical condition that is marked by the excessive growth of the epidermis, along with the presence of redness and scales. It is estimated to afflict around 1-3% of the global population. Certified Thai traditional physicians commonly prescribe a formula, which is a mixture of plant species, rooted in Thai traditional medicine. This practice aims to optimize therapeutic efficacy while minimizing the occurrence of adverse effects[46]. Traditional healers frequently use medicinal plants to treat a variety of illnesses, including psoriasis, as they are thought to be safe for human health[47]. In order to cure skin infections and other inflammatory illnesses, the herbal plant *Fernandoa adenophylla* has been employed. The goal of the current study was to confirm the plant *Fernandoa adenophylla*'s ability to treat psoriasis. *Fernandoa adenophylla* was subjected to phytochemical examination, and the results showed the presence of flavonoids, tannins, saponins, polysaccharides and alkaloids, glycosides, and steroids in pretty significant amounts. Therefore, the presence of the aforementioned phytochemicals may be responsible for the plant's stated medical efficacy[48]. Actinic keratosis, external genital warts, and superficial basal cell carcinoma can all be treated with IMQ, a toll-like receptor-7/8 (TLR-7/8) agonist[49]. Regarding inflammatory infiltration, skin redness, thickness, and scaling, the IMQ-induced mouse model has been compared to human plaque-type psoriasis[50]. Methotrexate, cyclosporine, and

acitretin are examples of well-known traditional systemic medications that have been used as the initial line therapy for psoriasis[51]. Despite this, such drugs appear to have numerous serious drawbacks that some patients may not be able to tolerate throughout prolonged treatment[52]. New efficient and secure therapeutic techniques are therefore needed. Traditional herbal remedies are one option because they have proven to be less expensive than light therapy and other modern biological agents[53]. The goal of the current investigation was to determine if the conventional herbal remedy *Fernandoa adenophylla* could reduce the psoriasis-like dermatitis that mice developed after exposure to IMQ.

In the present investigation, it was observed that all mice subjected to IMQ treatment had notable manifestations of psoriatic plaques, including erythema, skin thickness, scaling, parakeratosis, and acanthosis. In our preliminary study, it was observed that the psoriasis-like symptoms exhibited noticeable diminution after a period of 7 days of IMQ treatment. The aforementioned findings align with prior scholarly investigations that have documented the presence of instability in the psoriasis-like model caused by IMQ, mostly attributed to the adaptive response of the mouse skin to IMQ stimulation[43]. Ketoconazole was employed as a benchmark medicine for the purpose of comparing the antipsoriatic properties of *Fernandoa adenophylla*. The PASI grading of mice treated topically with extract decreased significantly, suggesting that FA may have anti-psoriatic efficacy in the Imiquimod-induced psoriatic mouse model. Histopathological analysis of skin from psoriatic mice showed a restoration of the normal structure of the skin and a dramatic reduction in hyperkeratinization after FA therapy. Psoriasis is characterized by an abnormally high rate of keratinocyte growth, which has been linked to the accumulation of macrophages in psoriatic skin lesions and their subsequent production of cytokines such as tumor necrosis factor-alpha (TNF- α), interleukin-1 beta, and interleukin-6. As a result, suppressing macrophage activity continues to be a promising avenue for treating psoriasis. Involved in the etiology of psoriasis and inducing the keratinocytes to secrete proinflammatory cytokines (such as IL-1, IL-6, and IL-17), TNF- α is one of the key inflammatory cytokines generated by macrophages[54]. It has long been known that interleukin (IL)-1, IL-6, and IL-17 all play a role in Th17 activation and differentiation[55]. This research showed that topical administration of FA dramatically reduced expression of tumor necrosis factor alpha, interleukin-1 beta, interleukin-6, and interleukin-17 in skin lesions, which in turn reduced Th17-associated inflammation and skin lesions. The findings of the study indicated that there was no statistically significant disparity in the levels of inflammatory cytokines, phenotypical observations, and histological discoveries between the mice treated with ketoconazole and those treated with the extract[56]. The discovery suggests that *Fernandoa adenophylla* holds significant potential as a therapeutic option within the range of treatments available for psoriasis. The findings of the molecular modelling studies indicated that the quality and correctness of protein structure for the residues lying in the Ramachandran favored region. The results of the molecular docking study clearly show that the Lapachone and Peshawaraquinone possess the essential structural features required to interact with the active site amino acids and this makes these compounds suitable candidate for the inhibition of the 4O1Z receptor. Alpha-lapachone and peshawaraquinone, two molecules evaluated for their ADME properties, exhibit distinct characteristics that can significantly impact their pharmacokinetic behavior and potential as drug candidates. Alpha-lapachone, with its higher molecular weight and greater hydrogen bonding capacity, presents a profile suggestive of robust interactions with biological targets. Its moderate lipophilicity, indicated by a positive Log P value, further supports its potential for traversing biological membranes. Similarly, peshawaraquinone, despite its lower molecular weight and fewer hydrogen-bonding sites, demonstrates favourable attributes, including a positive Log P value, indicating sufficient lipophilicity. Moreover, the absence of ADME violations in both molecules suggests compliance with established drug-likeness criteria. The observed improvements in PASI scores and histopathology may result from multi-target modulation by lapachone and peshawaraquinone. As illustrated in Figure 5, these compounds are likely to inhibit COX-1-mediated prostaglandin synthesis, downregulate NF-κB/JAK/STAT signalling, and reduce Th17-driven cytokine release, thereby restoring epidermal homeostasis. These findings collectively underscore the promising pharmacokinetic profiles of alpha-lapachone and peshawaraquinone, warranting further investigation into their therapeutic potential and mechanisms of action in relevant biological contexts, and toxicity studies like carcinogenicity, hepatotoxicity, mutagenicity, immunotoxicity and cytotoxicity were performed for better results. However, additional research into the molecular mechanisms of action in all facets is necessary to validate the efficacy and specificity of using *Fernandoa adenophylla* for the management of psoriasis in patients.

## Study Limitations & Future Perspectives

While the present study demonstrates the anti-psoriatic efficacy of *Fernandoa adenophylla* extracts, certain limitations must be acknowledged. Cytokine expression levels (e.g., TNF-α, IL-6, IL-17, IL-23) and transcription factor activation (e.g., NF-κB, STAT3) were not directly quantified, which would provide deeper mechanistic insights. Additionally, long-term safety, dermal absorption, and stability studies were beyond the scope of this investigation. Future work should include in vitro assays on keratinocytes and immune cell lines, followed by clinical pilot trials to validate efficacy in human subjects. Development of standardized extract formulations and evaluation in chronic


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psoriasis models will be essential steps toward clinical translation.

## Conclusions

The present study successfully demonstrates the significant anti-psoriatic potential of *Fernandoa adenophylla* extracts through a comprehensive in vitro, in vivo, and in silico approach. Phytochemical screening confirmed the presence of key bioactive constituents such as lapachone and peshawaraquinone, which are known for their anti-inflammatory and immunomodulatory properties. In the imiquimod-induced psoriasis mouse model, both leaf and fruit extracts, particularly at higher doses, effectively reduced clinical symptoms of psoriasis including erythema, scaling, and epidermal thickening. These therapeutic outcomes were further validated by histopathological analysis, which showed near-complete restoration of normal skin architecture in treated groups. Molecular docking studies revealed strong binding interactions between the identified compounds and the Cyclooxygenase-1 (4O1Z) protein, supporting their mechanistic role in modulating inflammatory pathways. Additionally, ADME and toxicity profiling suggested favorable pharmacokinetic attributes and safety profiles of the compounds, reinforcing their potential as drug candidates.

Collectively, these findings highlight *Fernandoa adenophylla* as a promising source of phytotherapeutic agents for the management of psoriasis. Future studies should focus on elucidating the molecular mechanisms in human models and exploring formulation development for clinical applications.

## Translational Significance

The favorable safety profile, multi-target anti-inflammatory effects, and COX-1 binding affinity of *F. adenophylla* extracts position them as promising phytopharmaceutical candidates for psoriasis management. Their potential for formulation into topical nanoemulsions or hydrogels could enhance skin penetration and therapeutic efficacy. Given the cost and side-effect profile of biologics, such standardized plant-based therapies could provide accessible alternatives, particularly in resource-limited settings**.**

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## Declarations

### Ethical Approval

All experimental procedures involving animals were conducted in accordance with ethical guidelines and regulations set by the Institutional Animal Ethics Committee (IAEC). Approval for this study was obtained from the IAEC of NIMS University Rajasthan, under protocol number 1302/PO/RE/S/09/CPCSEA. All efforts were made to minimize animal suffering, and experimental procedures were performed following the principles outlined in the Guide for the Care and Use of Laboratory Animals and in compliance with national and institutional regulations. Animals were housed in a controlled environment with standard food and water access, and human endpoints were established to ensure their well-being.

## Competing Interests

The authors declare that there are no competing interests.

## Author's Contributions

**RY**: Conceptualization, Methodology, Investigation and Validation, Data Curation, Writing - Original Draft. **TY:** Conceptualization, Supervision, Visualization, Methodology, Data Curation, Writing - Original Draft, Writing - Review & Editing, Resource, Study Design, Investigation and Validation. **AU:** Conceptualization, Supervision, Software, Visualization, Writing - Review & Editing, Investigation and Validation**. VK**: Formal analysis, Investigation and Validation, Statistical analysis, and proofreading. **PS**: Data Curation, Statistical analysis, Docking analysis**. SK**: Data Curation, Statistical analysis, Docking analysis**.**

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## Availability of Data and Material

Data included in this manuscript can be available upon request from the corresponding author.

## Consent for Publication

Not applicable

## List of Abbreviations

**FA:** *Fernandoa Adenophyllum* (FA)

**PASI:** *Psoriasis Area Severity Index*

**TNF-α:** Tumor necrosis factor-alpha

**PsA:** Psoriatic arthritis

**PGE2:** prostaglandin E2

**WHO:** World Health Organisation

**KTZ:** ketoconazole

**H&E:** Haematoxylin and eosin

**ELISA**: Enzyme-linked immunoassay

**HC**: Hedyotis corymbosa

**IMQ**: Imiquimod

**IL**: Interleukin

**MCP-1**: monocyte chemotactic protein 1

**TNF**: Tumour Necrosis Factor

**IL-1:** interleukin-1

## Conflict of Interest

None

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