EAS Journal of Biotechnology and Genetics
Abbreviated Key Title: EAS J Biotechnol Genet
ISSN: 2663-189X (Print) & ISSN: 2663-7286 (Online)
Published By East African Scholars Publisher, Kenya

OPEN ACCESS

Volume-8 | Issue-2 | Apr-Jun-2026 | DOI: https://doi.org/10.36349/easjbg.2026.v08i02.004

Original Research Article

In Silico Study of Natural Kinase3 (JAK3) Inhibitors for the Development of Herbal Topical Cosmetics for Skin Allergies

Muskan[1], Arya Ji[1], Manoj Kumar Sharma[1], Sachin Kumar[1]*

[1]Department of Bioinformatics, JV College, Baraut (Baghpat), Uttar Pradesh, India

Article History
Received: 16.04.2026
Accepted: 12.06.2026
Published: 15.06.2026

Journal homepage:
https://www.easpublisher.com

Quick Response Code

Abstract: Inflammatory skin allergies, including atopic dermatitis, allergic contact dermatitis, and urticaria, represent a significant global health burden affecting millions of individuals worldwide. The Janus kinase 3 (JAK3), a critical member of the JAK-STAT signaling pathway, has emerged as a promising therapeutic target due to its selective expression in immune cells and its pivotal role in mediating cytokine-driven inflammation. While synthetic JAK inhibitors have demonstrated clinical efficacy, their systemic immunosuppressive effects, hepatotoxicity, and high costs limit their widespread application. This study presents a comprehensive in silico approach to identify, characterize, and evaluate natural product-based JAK3 inhibitors as safer alternatives for topical management of skin allergies. Using the Protein Data Bank (PDB ID: 7C3N) as the target receptor, we performed database screening via IMPPAT and Dr. Duke's Phytochemical and Ethnobotanical Databases to identify medicinal plants with established anti-allergic and anti-inflammatory properties. From an initial pool of over 1,500 plants, seven medicinally important species—Aloe vera, Ocimum sanctum, Cucumis sativus, Azadirachta indica, Withania somnifera, Cocos nucifera, and Lawsonia inermis—were selected based on local availability and accessibility. Phytochemical profiling yielded 92 phytoconstituents, which were subjected to molecular docking analysis using Schrodinger Maestro 12.5 against the delgocitinib binding site of JAK3. The docking results revealed cucurbitacin-C (docking score: -12.406), quercetin (-9.98), luteolin (-9.243), and chrysophanic acid (-9.015) as top-scoring candidates with binding affinities comparable to the standard drug delgocitinib (-12.406). ADMET and physicochemical profiling via pKCSM and SwissADME demonstrated that all lead compounds adhered to Lipinski's Rule of Five and Veber's rules, indicating favorable drug-likeness, oral bioavailability, and safety profiles. The identified phytoconstituents exhibited robust hydrogen bonding and hydrophobic interactions within the ATP-binding pocket of JAK3, suggesting competitive inhibition mechanisms. These findings establish a pharmacoinformatics framework for the rational design of phytoconstituent-enriched herbal topical formulations and provide a foundation for downstream in vitro and in vivo validation of natural JAK3 inhibitors in inflammatory skin disease management.

Keywords: JAK3 Inhibitors, Natural Products, Phytoconstituents, Skin Allergy, Atopic Dermatitis, Molecular Docking, ADMET, *In Silico* Screening, Herbal Formulation.

INTRODUCTION

The skin, as the body's largest organ and primary interface with the external environment, serves as a critical barrier against pathogens, chemicals, ultraviolet radiation, and physical injury. Beyond its protective function, the skin actively participates in thermoregulation, water conservation, vitamin D synthesis, and sensory perception. However, this resilient barrier is susceptible to disruption by environmental pollutants, harsh weather conditions, microbial infections, immune system dysregulation, and genetic predisposition. When the skin barrier becomes compromised, allergens, irritants, and pathogens can

***Corresponding Author:** Sachin Kumar
Department of Bioinformatics, JV College, Baraut (Baghpat), Uttar Pradesh, India

penetrate the epidermis, triggering inflammatory cascades that manifest as dryness, erythema, pruritus, and the development of chronic skin conditions such as eczema, dermatitis, and psoriasis. The global prevalence of allergic skin diseases has risen dramatically over recent decades, with atopic dermatitis alone affecting approximately 15-20% of children and 1-3% of adults worldwide, imposing substantial physical, psychological, and economic burdens on affected individuals and healthcare systems.

Current therapeutic strategies for inflammatory skin diseases primarily rely on topical corticosteroids, systemic immunosuppressants, biologics, and phototherapy. While these interventions provide symptomatic relief, they are associated with significant limitations. Topical corticosteroids, the mainstay of anti-inflammatory treatment, can induce skin atrophy, striae, telangiectasia, and increased susceptibility to infections with prolonged use. Systemic immunosuppressants such as methotrexate and cyclosporine carry risks of hepatotoxicity, nephrotoxicity, and reactivation of latent infections. Biologic agents, though more targeted, are prohibitively expensive and require parenteral administration, while phototherapy demands frequent clinic visits and carries long-term risks of photoaging and skin malignancy. These drawbacks underscore the urgent need for safer, more accessible, and cost-effective therapeutic alternatives that can modulate inflammatory pathways without compromising systemic immune function.

The Janus kinase-signal transducer and activator of transcription (JAK-STAT) signaling pathway represents a central molecular communication network that transduces cytokine signals from the cell membrane to the nucleus, thereby regulating gene expression, immune cell activation, and inflammatory responses. Among the four members of the JAK family (JAK1, JAK2, JAK3, and TYK2), JAK3 exhibits a unique and restricted expression pattern, being predominantly localized to hematopoietic cells, particularly B and T lymphocytes, natural killer cells, and mast cells. This selective tissue distribution makes JAK3 an exceptionally attractive therapeutic target for immune-mediated inflammatory diseases, as its inhibition can dampen pathological cytokine signaling while sparing the broader physiological functions mediated by ubiquitously expressed JAK isoforms. In the context of skin allergies, JAK3 is activated downstream of interleukin receptors (IL-2, IL-4, IL-7, IL-9, IL-15, and IL-21), driving STAT phosphorylation, nuclear translocation, and the transcription of pro-inflammatory genes, chemokines, and mast cell mediators that perpetuate the allergic inflammatory cycle.

Natural products have served as the cornerstone of traditional medicine for millennia and continue to provide a rich reservoir of bioactive compounds with diverse pharmacological activities. Plant-derived phytochemicals, including flavonoids, alkaloids, terpenoids, and polyphenols, have demonstrated significant anti-inflammatory, immunomodulatory, and antioxidant properties with favorable safety profiles compared to synthetic drugs. The advent of computational biology and pharmacoinformatics has revolutionized natural product drug discovery, enabling high-throughput virtual screening, molecular docking, and ADMET (Absorption, Distribution, Metabolism, Excretion, and Toxicity) prediction to rapidly identify promising lead compounds and prioritize them for experimental validation. This study leverages an integrated in silico pipeline combining database mining, molecular docking, and ADMET profiling to systematically identify and characterize natural product-based JAK3 inhibitors from Indian medicinal plants, with the ultimate goal of developing a phytoconstituent-enriched herbal topical formulation for the management of inflammatory skin allergies.

Experimental Section

This study employed a systematic computational biology workflow to identify, characterize, and evaluate natural product-based JAK3 inhibitors for topical management of skin allergies. The methodology proceeded sequentially through database screening, phytoconstituent identification, ligand preparation, receptor preparation, molecular docking, and ADMET prediction.

Database Screening and Plant Selection

The identification of medicinal plants with anti-allergic and anti-inflammatory properties was conducted using two comprehensive databases: the Indian Medicinal Plants, Phytochemistry and Therapeutics (IMPPAT) database and Dr. Duke's Phytochemical and Ethnobotanical Databases. The IMPPAT database was queried using the search term "skin diseases" under the therapeutic use category, yielding an initial list of over 1,500 medicinal plants with documented dermatological applications. From this extensive dataset, seven plants were selected based on the following criteria: (i) established traditional use in skin disease management, (ii) local availability and accessibility for formulation development, (iii) diverse phytochemical profiles, and (iv) documented anti-inflammatory or immunomodulatory activity. The selected plants were Aloe vera (leaf), Ocimum sanctum (leaf), Cucumis sativus (fruit), Azadirachta indica (leaf), Withania somnifera (root and leaf), Cocos nucifera (endosperm), and Lawsonia inermis (leaf).

Phytoconstituent Identification and Ligand Preparation

Phytochemical profiling of the selected plants was performed using Dr. Duke's Phytochemical and Ethnobotanical Databases. For each plant, the database was queried by plant name, and the resulting phytoconstituent lists were filtered by plant part and biological activity class. A total of 92 phytoconstituents

were identified across the seven selected plants: Aloe vera (20), Ocimum sanctum (15), Cucumis sativus (7), Azadirachta indica (5), Withania somnifera (26), Cocos nucifera (8), and Lawsonia inermis (16). The chemical structures of the identified phytoconstituents were retrieved from the PubChem database using their SMILES (Simplified Molecular Input Line Entry System) strings. The 2D structures were drawn using ChemDraw Ultra 15.0 and converted to 3D representations using Chem3D 15.0. Energy minimization was performed using the MM2 force field algorithm to obtain stable conformations suitable for molecular docking. The optimized ligands were saved in compatible formats (PDB, Mol2) for downstream docking analyses.

Target Receptor Preparation

The three-dimensional structure of the human JAK3 kinase domain in complex with the inhibitor delgocitinib was retrieved from the Protein Data Bank (PDB ID: 7C3N) at a resolution of 2.8 Angstroms. The receptor structure was prepared using Schrodinger Maestro 12.5 software. The protein preparation workflow included the assignment of bond orders, addition of hydrogen atoms, creation of disulfide bonds, filling missing side chains and loops using Prime, and optimization of hydrogen bond networks. The co-crystallized ligand delgocitinib was extracted to define the binding pocket, and a receptor grid was generated centered on the ATP-binding site with default parameters. The prepared receptor was validated by re-docking the co-crystallized ligand and confirming a root-mean-square deviation (RMSD) of less than 2.0 Angstroms between the docked and crystallographic poses.

Molecular Docking Analysis

Molecular docking of all 92 phytoconstituents against the prepared JAK3 receptor was performed using Schrodinger Maestro 12.5 with the Glide module. The docking protocol employed the standard precision (SP) mode for initial screening, followed by extra precision (XP) mode for the top-scoring candidates. Each ligand was docked into the delgocitinib binding site, and the docking scores, binding poses, and interaction patterns were analyzed. The standard drug delgocitinib was used as a positive control for comparative analysis. The docking scores were evaluated based on GlideScore (kcal/mol), with more negative values indicating stronger binding affinity. For the top-scoring phytoconstituents, 2D and 3D interaction diagrams were generated to visualize hydrogen bonds, hydrophobic interactions, pi-pi stacking, and salt bridges within the ATP-binding pocket.

ADMET and Physicochemical Profiling

The pharmacokinetic and drug-likeness properties of the top-scoring phytoconstituents were predicted using pKCSM (Pharmacokinetic Webserver) and SwissADME. The ADMET parameters evaluated included: (i) Absorption: Caco-2 permeability, human intestinal absorption, and skin permeability; (ii) Distribution: volume of distribution (VDss), blood-brain barrier (BBB) permeability, and central nervous system (CNS) permeability; (iii) Metabolism: cytochrome P450 substrate potential; (iv) Excretion: total clearance and renal OCT2 substrate potential; and (v) Toxicity: AMES mutagenicity, hepatotoxicity, and skin sensitization. Drug-likeness was assessed using Lipinski's Rule of Five (molecular weight < 500 Da, logP < 5, hydrogen bond donors < 5, hydrogen bond acceptors < 10) and Veber's rules (rotatable bonds < 10, polar surface area < 140 Angstroms squared). Compounds violating more than one Lipinski rule or failing Veber's criteria were flagged for further evaluation.

RESULTS AND DISCUSSION

The integrated in silico pipeline successfully identified, characterized, and evaluated a set of high-confidence natural product-based JAK3 inhibitor candidates. The results are presented sequentially, with integrated discussion of their pharmacological implications.

Medicinal Plant Selection and Phytochemical Profiling

Database screening via IMPPAT identified over 1,500 medicinal plants with documented activity against skin diseases. From this extensive dataset, seven plants were strategically selected based on local availability, traditional use in dermatology, and diverse phytochemical profiles. Aloe vera (Aloe barbadensis miller) is renowned for its anti-inflammatory, wound-healing, and moisturizing properties, with over 75 active compounds including anthraquinones, polysaccharides, and vitamins. Ocimum sanctum (Holy Basil, Tulsi) possesses potent immunomodulatory and anti-allergic activities attributed to eugenol, ursolic acid, and rosmarinic acid. Cucumis sativus (Cucumber) provides cooling, anti-irritant, and hydrating effects through cucurbitacins, flavonoids, and tannins. Azadirachta indica (Neem) exhibits broad-spectrum antimicrobial and anti-inflammatory properties mediated by azadirachtin, nimbin, and quercetin. Withania somnifera (Ashwagandha) demonstrates adaptogenic and immunomodulatory effects via withanolides and withaferin A. Cocos nucifera (Coconut) offers emollient and barrier-repair functions through medium-chain fatty acids and phenolic compounds. Lawsonia inermis (Henna, Mehndi) provides cooling, anti-inflammatory, and antimicrobial benefits through lawsone, gallic acid, and tannins. Phytochemical profiling via Dr. Duke's database yielded a total of 92 phytoconstituents across the seven selected plants, providing a robust chemical library for molecular docking analysis.

Molecular Docking and Binding Affinity Analysis

Molecular docking of all 92 phytoconstituents against the JAK3 ATP-binding pocket (PDB ID: 7C3N) revealed significant variation in binding affinities. The

top-scoring phytoconstituents and their docking scores are summarized in Table 1. Cucurbitacin-C, isolated from Cucumis sativus, emerged as the highest-scoring phytoconstituent with a GlideScore of -12.406 kcal/mol, equaling the binding affinity of the standard drug delgocitinib (-12.406 kcal/mol). This remarkable binding affinity suggests that cucurbitacin-C may function as a potent competitive inhibitor of JAK3, potentially blocking ATP access to the catalytic site. Quercetin, a flavonoid present in Azadirachta indica and Ocimum sanctum, scored -9.98 kcal/mol, forming multiple hydrogen bonds with the hinge region residues (Leu828, Glu903) and hydrophobic interactions with the glycine-rich loop. Luteolin, from Lawsonia inermis, scored -9.243 kcal/mol, exhibiting a binding mode characterized by pi-pi stacking with Phe831 and hydrogen bonding with Asp967. Chrysophanic acid, an anthraquinone from Aloe vera, scored -9.015 kcal/mol, demonstrating favorable van der Waals interactions within the hydrophobic pocket. Additional promising candidates included aloe emodin (-8.52 kcal/mol), emodin (-8.391 kcal/mol), folic acid (-8.391 kcal/mol), xanthones (-8.371 kcal/mol), and lawsone (-8.359 kcal/mol). The 2D and 3D interaction diagrams revealed that the top-scoring phytoconstituents engaged in robust hydrogen bonding with the hinge region (residues 828-830), hydrophobic interactions with the glycine-rich loop and activation loop, and pi-pi stacking with conserved aromatic residues, mimicking the binding pattern of delgocitinib.

ADMET and Drug-Likeness Evaluation

ADMET profiling of the top 10 phytoconstituents was conducted using pKCSM and SwissADME to assess their pharmacokinetic suitability for topical and systemic administration. All evaluated compounds demonstrated favorable absorption profiles, with human intestinal absorption percentages ranging from 42.976% (gallic acid) to 96.31% (chrysophanic acid). Caco-2 permeability values varied from -0.612 (quercetin) to 1.366 (lawsone), with most compounds exhibiting moderate to high intestinal permeability. Skin permeability values were consistently negative (-2.735 to -3.09), indicating favorable transdermal penetration potential for topical application. Distribution analysis revealed that none of the compounds crossed the blood-brain barrier (BBB permeability < 0.5), suggesting minimal CNS side effects. Volume of distribution (VDss) values ranged from -1.121 (gallic acid) to 0.478 (chrysophanic acid), indicating predominantly extracellular distribution consistent with topical application. Metabolism profiling showed that most compounds were substrates for P-glycoprotein (P-gp), suggesting potential for drug-drug interactions and efflux-mediated resistance. Excretion parameters indicated moderate to high total clearance values (0.199 to 0.643), with no compound acting as a renal OCT2 substrate, suggesting minimal nephrotoxicity risk. Drug-likeness assessment using Lipinski's Rule of Five revealed that all top-scoring compounds complied with the criteria, possessing molecular weights below 500 Da, logP values below 5, fewer than 5 hydrogen bond donors, and fewer than 10 hydrogen bond acceptors. Veber's rules were also satisfied, with rotatable bonds below 10 and polar surface areas below 140 Angstroms squared for most candidates. These results collectively indicate that the identified phytoconstituents possess favorable drug-like properties suitable for further development as topical therapeutics.

Structure-Activity Relationship and Mechanistic Insights

Analysis of the binding modes of top-scoring phytoconstituents within the JAK3 ATP-binding pocket revealed important structure-activity relationships. Cucurbitacin-C, with its tetracyclic triterpenoid scaffold, occupied the deep hydrophobic pocket formed by Leu828, Val882, Ala966, and Leu956, forming extensive van der Waals contacts and a single hydrogen bond with the backbone carbonyl of Glu903. The rigid steroid-like core of cucurbitacin-C provided optimal shape complementarity to the ATP-binding cleft, explaining its exceptional binding affinity. Quercetin and luteolin, both flavonoids with a C6-C3-C6 diphenylpropane skeleton, adopted a planar conformation that enabled pi-pi stacking with Phe831 and hydrogen bonding with the hinge region. The presence of multiple hydroxyl groups on the B-ring (quercetin) enhanced hydrogen bond formation but slightly reduced lipophilicity compared to the more hydrophobic chrysophanic acid. The anthraquinone scaffold of chrysophanic acid and aloe emodin facilitated intercalation between the glycine-rich loop and the hinge region, with the keto groups forming critical hydrogen bonds with Asp967 and Lys830. The diverse chemical scaffolds represented among the top-scoring compounds—triterpenoids, flavonoids, and anthraquinones—suggest multiple viable pharmacophores for JAK3 inhibition, providing a rich chemical space for lead optimization and structure-based drug design.

Comparative Analysis with Synthetic JAK Inhibitors

The identified natural product inhibitors were compared with clinically approved synthetic JAK inhibitors, including tofacitinib, ruxolitinib, baricitinib, upadacitinib, and delgocitinib. While synthetic inhibitors typically achieve sub-nanomolar IC50 values through optimized hydrogen bonding and hydrophobic interactions, they often suffer from poor selectivity profiles, with many first-generation inhibitors displaying pan-JAK inhibition that compromises immune surveillance and increases infection risk. In contrast, the natural product inhibitors identified in this study demonstrated comparable binding affinities (as evidenced by docking scores) with potentially improved selectivity profiles due to their unique chemical scaffolds and interaction patterns. Notably, cucurbitacin-C achieved a docking score equivalent to delgocitinib, the only JAK inhibitor specifically approved for topical use in atopic dermatitis, suggesting comparable potency. The

favorable ADMET profiles of the phytoconstituents, particularly their low BBB permeability and absence of renal OCT2 substrate activity, indicate a reduced risk of systemic toxicity compared to oral synthetic JAK inhibitors. Furthermore, the antioxidant and anti-inflammatory properties inherent to many of these phytoconstituents may provide synergistic benefits beyond JAK3 inhibition, including reduction of oxidative stress, enhancement of skin barrier function, and modulation of additional inflammatory pathways.

Implications for Topical Formulation Development

The findings of this study have direct implications for the development of phytoconstituent-enriched herbal topical formulations for skin allergy management. The seven selected medicinal plants represent a diverse botanical portfolio with complementary therapeutic activities: anti-inflammatory (Aloe vera, Azadirachta indica), immunomodulatory (Ocimum sanctum, Withania somnifera), cooling and anti-irritant (Cucumis sativus, Lawsonia inermis), and emollient and barrier-repair (Cocos nucifera). The top-scoring phytoconstituents—cucurbitacin-C, quercetin, luteolin, and chrysophanic acid—can be incorporated into cream, gel, or ointment bases at optimized concentrations to achieve therapeutic JAK3 inhibition at the site of application while minimizing systemic absorption. The favorable skin permeability profiles of these compounds, as predicted by pKCSM, support their suitability for transdermal delivery. The formulation strategy should consider the physicochemical properties of each phytoconstituent, including solubility, stability, and compatibility with excipients, to ensure product efficacy, safety, and shelf-life. Additionally, the synergistic interactions between multiple phytoconstituents from different plants may enhance overall therapeutic efficacy through multi-target modulation of the JAK-STAT pathway and complementary anti-inflammatory mechanisms.

Limitations and Future Perspectives

This computational study, while comprehensive, has several limitations that must be acknowledged. In silico predictions of binding affinity and ADMET properties remain theoretical approximations that require experimental validation through in vitro enzyme inhibition assays, cell-based cytokine signaling assays, and in vivo animal models of skin inflammation. The molecular docking scores, though informative, do not account for dynamic conformational changes in the JAK3 binding pocket, protein flexibility, and solvent effects that may influence actual binding energetics. Molecular dynamics simulations would provide a more accurate representation of ligand-receptor interactions over time. The ADMET predictions, while based on robust machine learning models, may not fully capture species-specific pharmacokinetic variations and individual patient differences in drug metabolism. Furthermore, the stability, bioavailability, and formulation compatibility of the identified phytoconstituents in complex herbal preparations require empirical evaluation. Despite these limitations, this study provides a rational, data-driven foundation for prioritizing natural product leads and designing targeted experimental validation studies. Future research should focus on: (i) in vitro JAK3 kinase assays to confirm inhibitory potency and selectivity, (ii) cell-based models of cytokine-stimulated keratinocytes and immune cells to evaluate functional inhibition of the JAK-STAT pathway, (iii) ex vivo skin penetration studies to assess topical bioavailability, and (iv) clinical trials to evaluate the safety and efficacy of phytoconstituent-enriched formulations in patients with atopic dermatitis and other inflammatory skin conditions.

CONCLUSION

This study presents a comprehensive in silico investigation of natural product-based JAK3 inhibitors for the management of inflammatory skin allergies. Through systematic database mining, molecular docking, and ADMET profiling, we identified a high-confidence set of phytoconstituents with potent JAK3 binding affinities and favorable pharmacokinetic properties. Cucurbitacin-C, quercetin, luteolin, and chrysophanic acid emerged as the most promising lead compounds, exhibiting docking scores comparable to the standard drug delgocitinib and satisfying all criteria for drug-likeness and safety. The seven selected medicinal plants—Aloe vera, Ocimum sanctum, Cucumis sativus, Azadirachta indica, Withania somnifera, Cocos nucifera, and Lawsonia inermis—provide a diverse and accessible botanical resource for formulation development. The identified phytoconstituents engage the JAK3 ATP-binding pocket through competitive inhibition mechanisms, forming robust hydrogen bonds, hydrophobic interactions, and pi-pi stacking interactions with conserved catalytic residues. Their favorable ADMET profiles, including low BBB permeability, moderate clearance, and absence of renal toxicity, support their suitability for topical administration with minimal systemic exposure. These findings establish a pharmacoinformatics framework for the rational design of phytoconstituent-enriched herbal topical formulations and provide a foundation for downstream in vitro and in vivo validation. As the global burden of allergic skin diseases continues to rise and the limitations of existing therapies become increasingly apparent, natural product-based JAK3 inhibitors offer a promising avenue for developing safer, more accessible, and culturally acceptable treatments for millions of affected individuals worldwide.

Acknowledgements

The authors gratefully acknowledge the computational resources, lab facilities of the Dept. of Bioinformatics, JV College Baraut, used for the current research work.

REFERENCES

- Ahmed, S. S., De, A., Sarda, A., Godse, K., & Dhar, S. (2023). JAK inhibitors in dermatology. Indian Journal of Skin Allergy, 2(1), 3-7.
- Alves de Medeiros, A. K., Speeckaert, R., Desmet, E., Van Gele, M., De Schepper, S., & Lambert, J. (2016). JAK3 as an emerging target for topical treatment of inflammatory skin diseases. PloS One, 11(10), e0164080.
- Archer, C. (2004). Functions of the skin. In Rook's Textbook of Dermatology (Vol. 1, pp. 4.9-4.10).
- Ben, W. (2001). Dr. Duke's Phytochemical and Ethnobotanical Databases. Choice Reviews Online, 38, 38-3317.
- Biharee, A., et al. (2023). Flavonoids as promising anticancer agents: An in silico investigation of ADMET, binding affinity by molecular docking and molecular dynamics simulations. Journal of Biomolecular Structure and Dynamics, 41(16), 7835-7846.
- Biharee, A., et al. (2024). An amalgamated molecular dynamic and Gaussian based 3D-QSAR study for the design of 2,4-thiazolidinediones as potential PTP1B inhibitors. Journal of Molecular Graphics and Modelling, 127, 108695.
- Biharee, A., et al. (2024). A comprehensive study on natural products and their bioactive constituents to cure respiratory diseases. The Natural Products Journal, 14(2), 32-70.
- De Flora, S., & Bonanni, P. (2011). The prevention of infection-associated cancers. Carcinogenesis, 32(6), 787-795.
- Dong, X., et al. (2020). Aloe-emodin: a review of its pharmacology, toxicity, and pharmacokinetics. Phytotherapy Research, 34(2), 270-281.
- Fahmideh, H., et al. (2022). The role of natural products as inhibitors of JAK/STAT signaling pathways in glioblastoma treatment. Oxidative Medicine and Cellular Longevity, 2022, 7838583.
- Guttman-Yassky, E., & Krueger, J. G. (2017). Atopic dermatitis and psoriasis: two different immune diseases or one spectrum? Current Opinion in Immunology, 48, 68-73.
- Habif, T. P., Campbell, J. L., Dinulos, J. G., Chapman, M. S., & Zug, K. A. (2011). Skin disease e-book: diagnosis and treatment. Elsevier Health Sciences.
- Haykal, D., Lim, H. W., Calzavara-Pinton, P., Fluhr, J., Cartier, H., & Berardesca, E. (2025). The Impact of Pollution and Climate Change on Skin Health: Mechanisms, Protective Strategies, and Future Directions. JAAD Reviews, 6, 1-11.
- He, Q., et al. (2024). Janus kinase inhibitors in atopic dermatitis: an umbrella review of meta-analyses. Frontiers in Immunology, 15, 1342810.
- Howell, M. D., Kuo, F. I., & Smith, P. A. (2019). Targeting the Janus kinase family in autoimmune skin diseases. Frontiers in Immunology, 10, 2342.
- Huang, I. H., Chung, W. H., Wu, P. C., & Chen, C. B. (2022). JAK-STAT signaling pathway in the pathogenesis of atopic dermatitis: An updated review. Frontiers in Immunology, 13, 1068260.
- Kaplan, Y. C., Ozsarfati, J., Etwel, F., Nickel, C., Nulman, I., & Koren, G. (2015). Pregnancy outcomes following first-trimester exposure to topical retinoids: a systematic review and meta-analysis. British Journal of Dermatology, 173(5), 1132-1141.
- Korting, H. C., & Schafer-Korting, M. (2009). Carriers in the topical treatment of skin disease. Drug Delivery, 435-468.
- Krishna, P., Subhan, A., Gupta, K., Biharee, A., & Thareja, S. (2025). Natural Products in the 21st Century: Revolutionizing Therapeutics With Flavonoids as Key Phytometabolites. Phytotherapy Research, 39(9), 3833-3867.
- Malemud, C. J., & Pearlman, E. (2009). Targeting JAK/STAT signaling pathway in inflammatory diseases. Current Signal Transduction Therapy, 4(3), 201-221.
- Mohanty, S., et al. (2024). IMPPAT 2.0: An enhanced Indian Medicinal Plants, Phytochemistry and Therapeutics database. Scientific Reports, 14, 4689.
- Morris, R., Kershaw, N. J., & Babon, J. J. (2018). The molecular details of cytokine signaling via the JAK/STAT pathway. Protein Science, 27(12), 1984-2009.
- Mtewa, A. G., Egbuna, C., Beressa, T. B., Ngwira, K. J., & Lampiao, F. (2021). Phytopharmaceuticals: Efficacy, safety, and regulation. In Preparation of Phytopharmaceuticals for the Management of Disorders (pp. 25-38). Elsevier.
- Savita, S. (2025). The Impact of Climate Change on Dermatological Conditions: Analyzing the Effects of UV Exposure and Pollution. Scholar's Digest: Journal of Dermatology, 1(1), 59-78.
- Schwartz, D. M., Kanno, Y., Villarino, A., Ward, M., Gadina, M., & O'Shea, J. J. (2017). JAK inhibition as a therapeutic strategy for immune and inflammatory diseases. Nature Reviews Drug Discovery, 16(12), 843-862.
- Su, D., et al. (2019). Identification of Chinese herbal compounds with potential as JAK3 inhibitors. Evidence-Based Complementary and Alternative Medicine, 2019, 4982062.
- Sutterby, E., Thurgood, P., Baratchi, S., Khoshmanesh, K., & Pirogova, E. (2022). Evaluation of in vitro human skin models for studying effects of external stressors and stimuli and developing treatment modalities. View, 3(2), 20210012.
- Welsch, K., Holstein, J., Laurence, A., & Ghoreschi, K. (2017). Targeting JAK/STAT signalling in inflammatory skin diseases with small molecule inhibitors. European Journal of Immunology, 47(7), 1096-1107.

- Yang, W., et al. (2025). An exhaustive examination of the research progress in identifying potential JAK inhibitors from natural products: a comprehensive overview. Chinese Medicine, 20(1), 130.
- Yin, Q., Wang, L., Yu, H., Chen, D., Zhu, W., & Sun, C. (2021). Pharmacological effects of polyphenol phytochemicals on the JAK-STAT signaling pathway. Frontiers in Pharmacology, 12, 716672.

Cite This Article: Muskan, Arya Ji, Manoj Kumar Sharma, Sachin Kumar (2026). *In Silico* Study of Natural Kinase3 (JAK3) Inhibitors for the Development of Herbal Topical Cosmetics for Skin Allergies. *EAS J Biotechnol Genet, 8*(2), 29-35.