Network Pharmacology of Plumbagin for the Treatment of Psoriasis

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ABSTRACT

Background: Psoriasis skin disease brings attention to pharmacology studies; many traditional medicines from plants are defined as promising candidates for this disease treatment. Plumbagin is one candidate that has been proven for several decades for these issues.

Methods: The potency of Plumbagin as an anti-psoriasis treatment was analyzed using WAY2DRUG PASS Prediction. Target proteins prediction was analyzed using Pass Protein Target, DIGEP-Pred, and Comparative Toxicogenomic Database. Targets related to Psoriasis were obtained from The Human Gene Database Genecards, Open Target, and PharmGKB. The JVENN tol was used to visualize the Venn Diagram. Protein-protein interaction was analyzed using STRING DB V.12 and the filtered by Cytoscape V.10.1. Functional annotation was analyzed using DAVID.

Results: Plumbagin can target proteins interacting with Psoriasis-related proteins such as TP53, CASP3, MAPK3, TNF, AKT1, STAT3, MAPK8, NFKB1, ESR1, and EP300.

Conclusions: Plumbagin has good potential as an anti-psoriasis agent.

Keywords: Bio-informatics; Network Pharmacology; Psoriasis; Plumbagin.

INTRODUCTION

Psoriasis is a skin disease with symptoms of chronic thickened, non-itchy, scaly skin requiring continuous therapy (1). Continuous use of steroids or cytostatic drugs such as Methotrexate can cause various side effects for the body (2). As an alternative, biological therapies such as anti-TNF alpha or anti-IL-17 are now famous as Psoriasis treatments (3). However, the price is still relatively expensive for the Indonesian population and not covered by national health insurance.

Another available alternative for Psoriasis treatment is herbal medicine (4). One Indonesian plant that has characteristics as an anti-proliferative agent is Ki Encok or *Plumbago zeylanica L*. Part of this plant that has been widely studied is its root, which contains the compound *Plumbagin* (5). *Plumbagin* has been studied to inhibit the proliferation of human B cell precursor leukemia cells, human lung adenocarcinoma, human colorectal adenocarcinoma, hepatocellular carcinoma cells and human epidermoid carcinoma in vitro (6,7). Our previous study reported no effect of the chloroform extract of P. zeylanica root on biomarkers Caspase-3, Cyclin-dependent kinase-2, cyclin A, and interleukin-23 in Imiquimod-induced Psoriatic mice (8). Indirect in vivo studies to identify potential biomarkers as targets for *Plumbagin* therapy are time-consuming and ineffective. Therefore, conducting an in-silico study to assess the target proteins affected by *Plumbagin* in Psoriasis is necessary.

The advance of technology creates many databases that can be used for computational method of pharmacognosy research (9). This method is promising in drug exploration

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and provide a prelude to clinical research (10). The time consuming, expensive budget, and sacrifice many animals are overcome in in silico method. Currently, in silico study is widely applied to find out whether a natural ingredient has a pharmacological effect before testing it on experimental animals. In silico testing steps can provide advantages in terms of costs, time, tools and materials (11).

Network pharmacology has been used to analyse the effect of traditional Chinese medicine (TCM) on Psoriasis (12,13). However, those studies did not propose the in vitro or in vivo study as the confirmation. Another studies proven that network pharmacology study can guide the selection of target proteins for in vivo study (14,15). The potential targets and pathways of *Smilax glabra Roxb*., a TCM, in the treatment of Psoriasis was first analysed using network pharmacology methods, followed by in vivo experimental verification, to study its potential mechanism. Among key targets in network pharmacology study, *Smilax glabra Roxb*. can regulate the T cell differentiation in Psoriasis, possibly by regulating the insulin receptor signaling pathway (14).

This study aims to identify *Plumbagin*'s therapeutic targets and inhibitory mechanisms in Psoriasis through network pharmacology based on bioinformatics. Previous research using network pharmacology between *Plumbagin* and hepatocellular carcinoma showed that the therapeutic target was to increase reactive oxygen species (ROS) production and regulate the PI3K/Akt and MAPK pathways (7). The results of this network pharmacology are expected to identify the therapeutic targets of *Plumbagin* in the inflammatory and proliferation pathways in the pathogenesis of Psoriasis.

MATERIALS AND METHODS

The steps we execute in this network pharmacology are as follows (Figure 1)

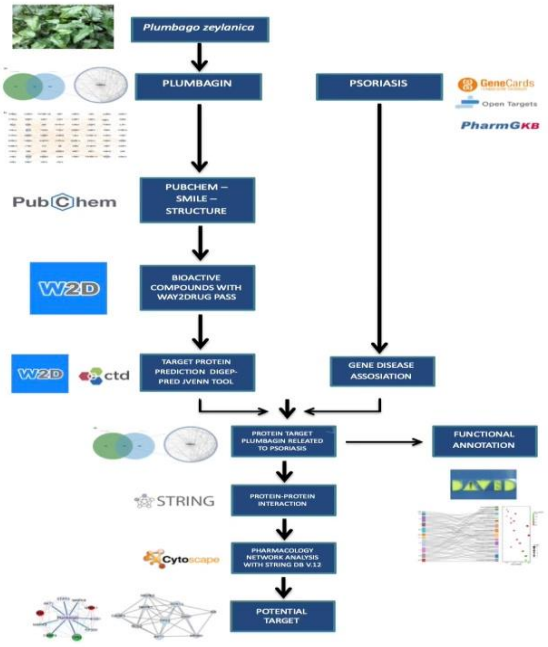


Figure 1. Network pharmacology workflow

Step 1. *Plumbagin* Profile Search

The PubChem database online sources (https://pubchem.ncbi.nlm.nih.gov/) was used for the simplified molecular-input line-entry system (SMILE) search and the structure of *Plumbagin*.

Step 2. Prediction of Bioactive Compounds Activity

The potential of *Plumbagin* as an anti-psoriasis treatment was analyzed using WAY2DRUG PASS prediction (http://www.pharmaexpert.ru/passonline/predict.php). WAY2DRUG Pass Prediction uses Structure Analysis Relationship (SAR) analysis to compare the *Plumbagin* and other compounds which are already known to have specific potential as an anti-psoriasis treatment. The Probability to be Active (Pa) value is the predicted value of WAY2DRUG PASS, which describes the potential of *Plumbagin*. The higher the Pa value of a function, the better the level of accuracy (16).

Step 3. Prediction of Target Proteins

Target proteins prediction analysis was obtained from the Pass Protein Target (https://www.way2drug.com/passtargets/), DIGEP-Pred (https://www.way2drug.com/ge/), and Comparative Toxicogenomic Database (https://ctdbase.org/). Cut off score used was 0.3 (range 0 - 1). Target prediction is obtained by entering the SMILE that has been found in Step 1.

Targets related to Psoriasis were obtained from The Human Gene Database Genecards (https://www.genecards.org/) (17), Open Target (https://platform-docs.opentargets.org/) (18), & PharmGKB (https://www.pharmgkb.org/) (19). Targets related to disease are then mapped using a Venn diagram to determine the intersection of targets. The JVENN tool (https://jvenn.toulouse.inrae.fr/app/index.html) was used to visualize the data as a Venn diagram (20).

Step 4. Pharmacology Network Analysis

Intersection targets in Step 3 were then analyzed for protein-protein interaction using the STRING DB V.12 database (https://string-db.org/) using the following parameters; Organism: Homo sapiens, Network type: complete STRING network, Score: High confidence interaction (0.9), and FDR stringency medium 5 percent (21). The tsv format of the STRING output was then further processed using Cytoscape V.10.1. Filtering data to get the top 10 target nodes based on degree centrality (DC), betweenness centrality (BC), and closeness centrality (CC) values with cut-off DC 3, BC 0.044, and CC 0.374.

Calculations of DC are made based on shortest path analysis, namely by looking at the values of CC and BC. BC describes the potential of a protein in the communication flow. Protein nodes with high BC values are considered interesting because they have a role as communication mediators and can control the flow of information. CC estimates how fast information flows through a particular node to other nodes. Nodes with high CC values are easily accessible. The use of DC, BC, and CC is to see the role of a node in the network based on its ability to interact with other nodes in the network or act as a bridge for information flow between other nodes (22).

Step 5. Functional Annotation

Database for Annotation, Visualization, and Integrated Discovery (DAVID) (https://david.ncifcrf.gov/) was used to determine the function of the gene that has been found in the intersection of the Venn diagram (20). The annotations used refer to Gene Ontology (https://geneontology.org/).

RESULTS

Prediction of *Plumbagin* Activity with SAR Approach

Based on the search for *Plumbagin* activity based on the SAR approach, *Plumbagin* has good potential as a TP53 expression enhancer (prediction score = 0.744) and MMP9 expression inhibitor (prediction score = 0.726). *Plumbagin* has lower potential for inhibits the nuclear factor kappa beta (prediction score = 0.232) and as an interferon antagonist (prediction score = 0.165) in Psoriasis pathways (Figure 2).

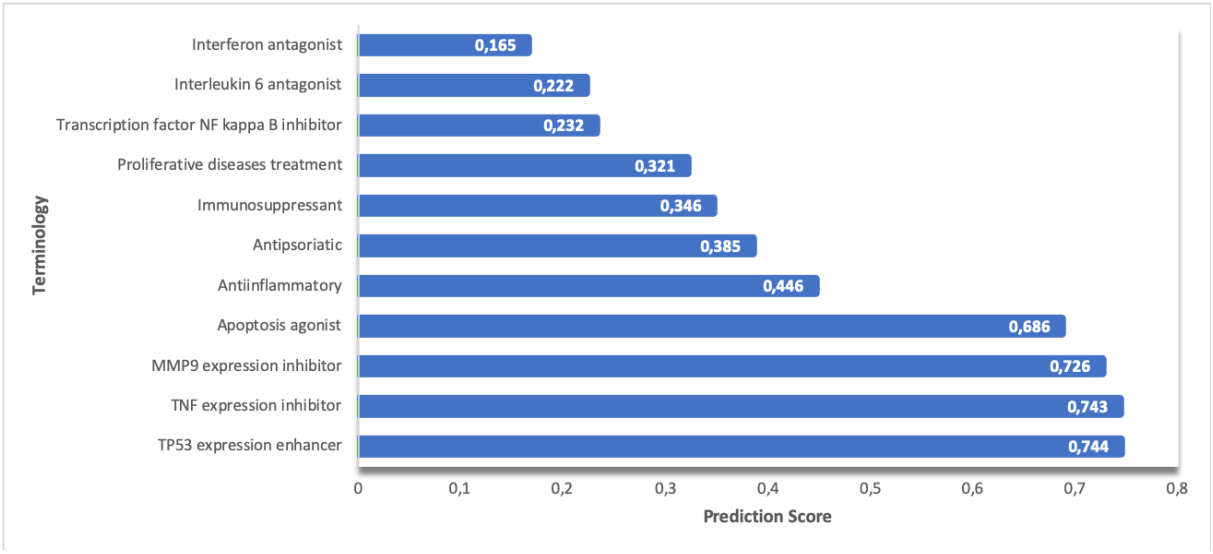
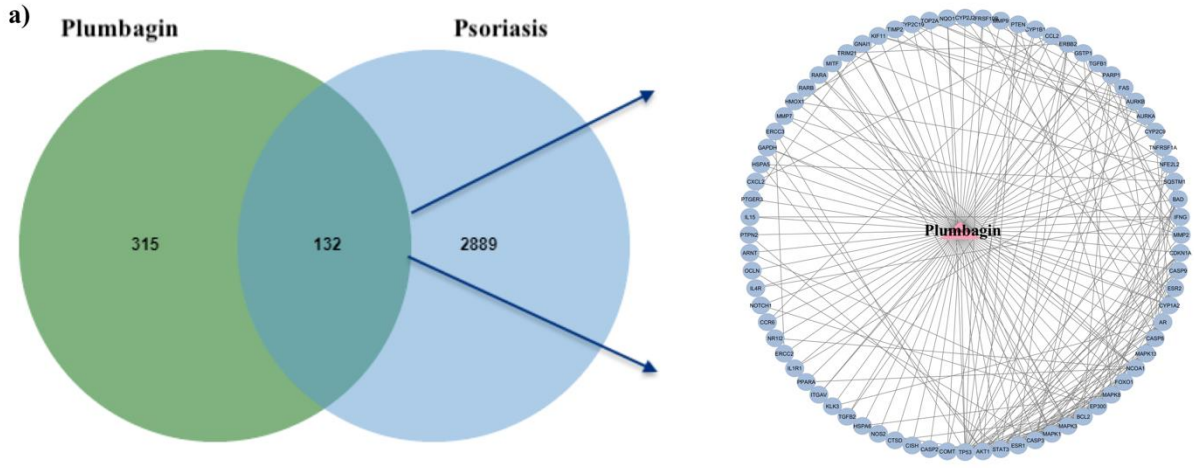


Figure 2. Potential pathways as targets for *Plumbagin* therapy based on SAR approach

Target Protein Prediction

Based on analysis using the CTD database and Way2Drug Database, *Plumbagin* can interact with 447 targets. There are 3021 targets associated with Psoriasis that we managed to get from the compilation of PharmGKB, Genecards, and OpenTarget databases. Of the 447 *Plumbagin* targets and 3021 Psoriasis targets, 132 targets overlap between *Plumbagin* and Psoriasis (Figure 3a). Based on analysis of the Cytoscape program, target proteins TP53, AKT1, and STAT3 are the top 3 proteins with the biggest blue circle (represent Degree). The bigger the circle, the higher the degrees (Figure 3b).



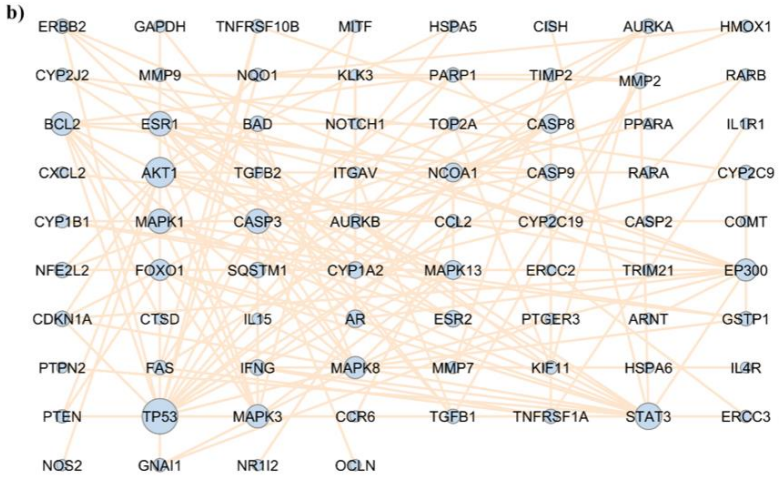


Figure 3. (a) Venn diagram of common targets of *Plumbagin* in Psoriasis. (b) *Plumbagin* therapeutic targets associated with Psoriasis. Blue circles represent the number of proteins interacting with another protein (Degree). Edges represent protein-protein interactions.

Pharmacology Network Analysis

Data filtering was performed to obtain the top 10 targets of *Plumbagin* with psoriasis which are TP53, AKT1, STAT3, ESR1, CASP3, MAPK1, BCL2, MAPK8, EP300, AR (Table 1). TP53 has the highest degree, relatively high BC, and comparable CC value to other targets. Higher CC means that TP53 has better position in the protein network and lower BC means that TP53 is not really good as mediator of information between target proteins in the network. The degree value of TP53 protein is 23 means that there are 23 proteins that can interact with TP53.

Table 1. Network Centrality Score of top 10 *Plumbagin* Target for Psoriasis

Node	Degree	Betweenness Centrality (BC)	Closeness Centrality (CC)
TP53	23	0.29737233	0.416666667
AKT1	18	0.155056022	0.384615385
STAT3	15	0.35919286	0.409836066
ESR1	13	0.067358834	0.465838509
CASP3	13	0.082821308	0.446428571
MAPK1	13	0.064682727	0.433526012
BCL2	12	0.05177186	0.414364641
MAPK8	11	0.162121793	0.477707006
EP300	11	0.096422956	0.384615385
AR	7	0.047443421	0.414364641

Functional Annotation

Based on the functional annotation search using the Gene Ontology database on the DAVID server, it shows that TP53, STAT3, and AKT1 are *Plumbagin* targets that

play a role in many pathways. TP53 is involved in the positive regulation of apoptotic process, gene expression, response to oxidative stress, positive regulation of transcription from RNA polymerase II promoter, cellular response to DNA damage stimulus, positive regulation of transcription and DNA-templated, regulation of apoptotic process, negative regulation of apoptotic process, negative regulation of cell proliferation, and negative regulation of cell growth (Table 2).

STAT3 is enrolled in the positive regulation of gene expression, transcription from RNA Polymerase II promoter, signal transduction, cell migration transcription DNA-templated, inflammatory response, and regulation of cell proliferation (Table 2). While it also acts as a negative regulation of cell proliferation

AKT1 induce positive regulation of gene expression, response to oxidative stress, negative regulation of apoptotic process, positive regulation of transcription from RNA Polymerase II promoter, signal transduction, positive regulation of transcription DNA-templated, inflammatory response, regulation of apoptotic process, and positive regulation of cell proliferation (Table 2).

Table 2. Pathways affected by top10 targets of *Plumbagin* therapy (p value <0.01)

Pathways	Count	Genes
Positive Regulation of Apoptotic Process	24	NCOA1, TOP2A, TGFB1, BAD, MMP2, TNFRSF10B, MMP9, FOXO1, CASP9, MAPK8, CASP8, LGALS1, ERCC3, CASP3, SMPD1, BCL2, CASP2, FAS, CYP1B1, HMOX1, RARB, CTSD, SQSTM1, TP53
Apoptotic Process	24	PARP1, BAD, PTEN, TNFRSF10B, MMP9, FOXO1, AURKA, TNFRSF1A, CASP9, CASP8, LGALS1, IFNG, ERCC3, CASP3, ERCC2, BCL2, CASP2, FAS, EP300, MAPK1, RARB, SQSTM1, TP53, MAPK3
Positive Regulation of Gene Expression	21	NFAT5, TGFB1, NOTCH1, VDR, STAT3, NR1I2, PTPN22, MITF, ADAM19, AR, OCLN, MAPK8, IFNG, ERBB2, RARA, AKT1, MAPK1, GAS6, TP53, NFE2L2, MAPK3
Response to Oxidative Stress	11	NQO1, MAPK8, VNN1, ERCC3, CA3, ERCC2, KRT1, HMOX1, AKT1, TP53, NFE2L2
Negative Regulation of Apoptotic Process	19	NQO1, HSPA5, TSC22D1, GSTP1, PTEN, MITF, MMP9, FOXO1, AURKA, MAPK8, CASP3, CAT, ERBB2, BCL2, CASP2, FAS, AKT1, GAS6, TP53
Negative Regulation of Cell Proliferation	16	CDKN1A, TGFB2, TGFB1, NOTCH1, VDR, STAT3, PTEN, TOB1, AR, FABP3, RARA, CYP1B1, RARB, SPRY1, TP53, PTPN2
Positive Regulation of Transcription from RNA Polymerase II Promoter	26	TOP2A, NFAT5, NOTCH1, NR1I2, FOXO1, AKT1, EP300, MAPK3, NCOA1, TGFB1, PARP1, VDR, STAT3, ARNT, MITF, DEK, ESR1, ESR2, TNFRSF1A, AR, RARA, RARB, PPARA, SQSTM1, TP53, NFE2L2
Cellular Response to DNA Damage Stimulus	13	TOP2A, NFAT5, CDKN1A, PARP1, FOXO1, CASP9, UBE2T, CASP3, BCL2, CASP2, MAPK1, TP53, MAPK3
Signal Transduction	25	NFAT5, NR1I2, PLAU, OLFML3, SMPD1, ERBB2, CCL2, AKT1, MAPK1, CCR6, IL4R, IL15, TXNRD1, STAT3, TNFRSF10B, DEK, ESR1, ESR2, TNFRSF1A, AR, ITPKA, RARA, RARB, FAS, GAS6

Pathways	Count	Genes
Positive Regulation of Cell Migration	11	TGFB1, FLT1, CD151, NOTCH1, MMP7, HSPA5, PLAU, MMP2, STAT3, ITGAV, MMP9
Positive Regulation of Transcription, DNA-Templated	17	NCOA1, TGFB1, NOTCH1, STAT3, NR1I2, ARNT, MITF, ESR1, FOXO1, ESR2, AR, RARA, AKT1, EP300, PPARA, TRIM21, TP53
Inflammatory Response	13	TGFB1, NOS2, IL1R1, IL15, PTGER3, STAT3, CXCL2, TNFRSF1A, VNN1, CCL2, AKT1, RAC1, NFE2L2
Regulation of Apoptotic Process	10	CASP9, LGALS1, CASP8, RARA, CASP2, FAS, TNFRSF10B, AKT1, ESR1, TP53
Positive Regulation of Cell Proliferation	14	TGFB2, TGFB1, FLT1, NOTCH1, TSC22D1, IL15, PTEN, AR, IFNG, ERBB2, BCL2, RARA, AKT1, ITGAV
Regulation of Cell Proliferation	8	TGFB2, TGFB1, IL4R, NOS2, PLAU, ERBB2, STAT3, MITF
Negative Regulation of Cell Growth	7	NPPB, CDKN1A, TGFB2, TGFB1, BCL2, TP53, ESR2
Epithelial Cell Apoptotic Process	4	CASP9, CASP3, BCL2, HMOX1

DISCUSSIONS

The identified and discussed targets in this study are novel for Plumbagin as a treatment for Psoriasis. There are no previous studies examining the effects of Plumbagin on proteins involved in Psoriasis using network pharmacology. However, previous studies reported the TP53 as protein target for Plumbagin in cancer (23,24).

The TP53 protein, encoded by TP53 gene, is an important transcription factor that plays a central role in cell cycle regulation mechanisms and control of cell proliferation. The TP53 protein can trigger apoptosis, a process of programmed cell death, in response to DNA damage or other cellular stress. Apoptosis is an important defense mechanism that prevents the proliferation of damaged or abnormal cells. In this context, TP53 plays a role in the "positive regulation of apoptosis" because it can activate pathways that lead to apoptosis when needed. However, TP53 is also involved in the "negative regulation of apoptosis" in some contexts. This is because TP53 can induce the expression of genes that play a role in DNA repair or cell cycle arrest, which gives the cell a chance to repair the damage before entering the process of apoptosis. So, in situations where DNA damage can be repaired, TP53 helps stop or delay apoptosis to allow time for repair. Therefore, TP53 has a dual role in regulating apoptosis, depending on the context and cellular conditions. In some situations, it promotes apoptosis to eliminate damaged cells, while in other situations it inhibits apoptosis to allow DNA repair and cell recovery. This demonstrates the complexity and ingenuity of the cellular regulatory mechanisms involving TP53, which are critical for preventing cancer development and maintaining cellular homeostasis (25–27).

The possibility of increased p53 expression in psoriasis skin is a physiological reaction showing cells' physiological efforts to respond to proliferation and repair DNA damage (21). Research conducted by Kim et al. (2018) showed an equal distribution of p53 and Ki67-positive cells, which supports the hypothesis that increased proliferation increases the synthesis of the wild-type p53 (p53 WT) protein to prevent cell transformation into malignant malignancies (28). The current study showed that *Plumbagin* has the potential to act as a TP53 expression enhancer.

P53 WT plays a vital role in preventing carcinogenesis

(29). TP53 can help cells overcome over-proliferation, repair DNA damage, and prevent cell malignancy (29). The phosphatidylinositol 3-kinase (PI3K) and protein kinase B (AKT) signaling pathways play central roles in various cellular functions such as cell proliferation and survival. The PI3K/AKT signaling pathway negatively regulates the transcription factor fork head box O (FOXO) and may inhibit cell proliferation. PI3K signaling regulates keratinocyte proliferation by activating AKT and other targets and inducing FOXO downregulation. PI3K and AKT amplification and gradual loss of FOXO are recognized in psoriasis lesions (30). Psoriasis is a systemic inflammatory disease driven by T lymphocytes (31). Regulatory T cells (Treg) are essential for establishing and maintaining immune tolerance. Dysregulation of the protein kinase B(AKT)-FOXO1 pathway may be a critical cause of Treg dysfunction in Psoriasis (32).

Signal Transducer and Activator of Transcription (STAT) 3 has two roles, namely as a transcription activator and also as an oncogene that can cause cancer. As a transcription activator, STAT3 if activated and bound to the target gene can trigger gene expression (33). This protein plays a role in inhibiting the effects of the body's immune response that occurs when there are tumor cells (34). STAT3 has recently emerged as a critical player in the development and in the pathogenesis of Psoriasis and psoriasis-like inflammatory conditions. Benzo[b]thiophen-2-yl-3-bromo-5-hydroxy-5H-furan-2-one (BTH), a small molecule that acts as an anti-inflammatory agent, inhibits the release of several key psoriasis cytokines such as TNF, IL-8, IL-6, and CCL27 through downregulating NF-kB and disrupting signal transducer and activator of transcription phosphorylation 3 (STAT3) and its translocation to the nucleus, resulting in decreased keratinocyte proliferation. Topical administration of BTH prevents skin infiltration and hyperplasia by suppressing NF-kB and STAT3 phosphorylation (35).

Many studies have revealed an increased concentration of TNF-α in the serum of patients with Psoriasis and a correlation between serum TNF-α levels and disease severity. TNF-α was more beneficial than other tested cytokines as a follow-up marker to monitor disease severity (21). *Plumbagin* can potentially be a TNF expression inhibitor to prevent cell proliferation and excessive inflammation in psoriasis cases (36).

The increased expression of MMP-9 mRNA in non-lesion significant plaque skin compared to non-lesion small plaque skin in psoriatic skin suggests that increased MMP-9 mRNA expression is associated with large lesion size (37). In patients with Psoriasis, neutrophil-derived matrix metalloproteinase 9 (MMP-9) plays a vital role in vascular endothelial cell barrier dysfunction through extracellular signal-regulated kinase-1/2 and p38 pathways. Pharmacological inhibition of MMP-9 in two different models provided reductions in skin vasodilation, vascular permeability, and inflammation, suggesting MMP-9 is a target in the pathogenesis of Psoriasis (38). *Plumbagin* has the potential as an MMP9 expression inhibitor, which is expected with this potential to inhibit psoriasis pathogenicity.

CONCLUSION

Plumbagin showed a good potential to act as an anti-psoriasis agent. Future in vivo studies can determine the interactions between *Plumbagin* and Psoriasis-related proteins such as TP53, CASP3, MAPK3, TNF, AKT1, STAT3, MAPK8, NFKB1, ESR1, and EP300.

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CONFLICT OF INTEREST

All authors involved in this scientific publication declare there is no conflict of interest or affiliation with others.

REFERENCES

1. Chan T., Hawkes J. and Krueger J. Interleukin 23 in the skin: role in psoriasis pathogenesis and selective interleukin-23 blockade as treatment. *Ther. Adv. Chronic Dis.* 2018; 9(5):111–119.
2. Czarnecka-Operacz M. and Sadowska-Przytocka A. The possibilities and principles of methotrexate treatment of psoriasis: the updated knowledge. *Postep Dermatol. Alergol.* 2014; 31(6):392–400.
3. Frieder J., Kivelevitch D., Haugh I., Watson I. and Menter A. Anti-IL-23 and anti-IL-17 biologic agents for the treatment of immune-mediated inflammatory conditions. *Clin. Pharmacol. Ther.* 2017; 103(1):88–101.
4. Orch H., Chaachouay N., Douiri E. M., Faiz N., Zidane L. and Douira A. Use of medicinal plants in dermato-cosmetology: an ethnobotanical study among the population of Izarène. *Jordan J. Pharm. Sci.* 2021; 14(3):323–340.
5. Sundari B., Telapolu S., Dwarakanath B. and Thyagarajan S. Cytotoxic and antioxidant effects in various tissue extracts of *Plumbago zeylanica*: implications for anticancer potential. *Pharmacogn. J.* 2017; 9(5):706–712.
6. Ito C., Matsui T., Takano M., Wu T. and Itoigawa M. Anti-cell proliferation effect of naphthoquinone dimers isolated from *Plumbago zeylanica*. *Nat. Prod. Res.* 2018; 32(18):2127–2132.
7. Wei Y., Lin Y., Chen W., Liu S., Jin L. and Huang D. Computational and in vitro analysis of plumbagin's molecular mechanism for the treatment of hepatocellular carcinoma. *Front. Pharmacol.* 2021; 12:594833.
8. Purwoko M., Indarto D., Kariosentono H., Purwanto B., Soetrisno S. and Cilmiaty R. Chloroform extract of *Plumbago zeylanica* Linn. roots ameliorates the epidermal thickness of imiquimod-induced psoriatic mice through cell cycle and apoptosis. *Open Access Maced. J. Med. Sci.* 2022; 10(B):1129–1136.
9. Syahri J., Nurohmah B. A. and Yuanita E. Effectivity of remdesivir and some compounds as therapeutic potential drugs for anti-SARS-CoV-2: in silico study. *Jordan J. Pharm. Sci.* 2021; 14(1):49–62.
10. Thakre R., More A., Deshmukh P., Supekar B., Kshirsagar R., Navghare V. et al. Exploring anti-inflammatory targets of flavonoids through integrated molecular docking and network pharmacology. *Jordan J. Pharm. Sci.* 2025; 18(1):160–179.
11. Li L., Yang L., Yang L., He C., He Y., Chen L. et al. Network pharmacology: a bright guiding light on the way to explore the personalized precise medication of traditional Chinese medicine. *Chin. Med.* 2023; 18:146.
12. Guo S., Zhou J-Y., Tan C., Shi L., Shi Y. and Shi J. Network pharmacology-based analysis on the mechanism of action of *Ephedrae Herba–Cinnamomi Ramulus* couplet medicines in the treatment for psoriasis. *Med. Sci. Monit.* 2021; 27:e927421-1–e927421-14.
13. Yue C., Feng J. and Gao A. A network pharmacology and molecular docking investigation on the mechanisms of Shanyaotianhua decoction (STT) as a therapy for psoriasis. *Medicine*. 2023; 102(34):e34859.
14. Guo Y., Mao W., Bai N., Jin L., Tang S., Lin X. et al. Integrated network pharmacological analysis revealed that *Smilax glabra* Roxb. alleviates IMQ-induced psoriatic skin inflammation through regulating T-cell immune response. *J. Ethnopharmacol.* 2024; 325:117836.
15. Guo Y., Gan H., Xu S., Zeng G., Xiao L., Ding Z. et al. Deciphering the mechanism of Xijiao Dihuang decoction in treating psoriasis by network pharmacology and experimental validation. *Drug Des. Devel. Ther.* 2023; 17:2805–2819.
16. Ochoa D., Hercules A., Carmona M., Suveges D., Baker J., Malangone C. et al. The next-generation Open Targets Platform: reimagined, redesigned, rebuilt. *Nucleic Acids Res.* 2023; 51(D1):D1353–D1359.
17. Whirl-Carrillo M., Huddart R., Gong L., Sangkuhl K., Thorn C. F., Whaley R. et al. An evidence-based framework for evaluating pharmacogenomics knowledge for personalized medicine. *Clin. Pharmacol. Ther.* 2021; 110(3):563–572.
18. Bardou P., Mariette J., Escudié F., Djemiel C. and Klopp C. jvenn: an interactive Venn diagram viewer. *BMC Bioinformatics*. 2014; 15:293.

19. Szklarczyk D., Kirsch R., Koutrouli M., Nastou K., Mehryary F., Hachilif R. et al. The STRING database in 2023: protein–protein association networks and functional enrichment analyses for any sequenced genome of interest. *Nucleic Acids Res.* 2023; 51(D1):D638–D646.
20. Sherman B. T., Hao M., Qiu J., Jiao X., Baseler M. W., Lane H. C. et al. DAVID: a web server for functional enrichment analysis and functional annotation of gene lists (2021 update). *Nucleic Acids Res.* 2022; 50(W1):W216–W221.
21. Baran W., Szepietowski J. C. and Szybejko-Machaj G. Expression of p53 protein in psoriasis. *Acta Dermatovenerol. Alp. Pannon. Adriat.* 2005; 14(3):79.
22. Ashtiani M., Mirzaie M. and Jafari M. CINNA: an R/CRAN package to decipher central informative nodes in network analysis. *Bioinformatics*. 2019; 35(8):1436–1437.
23. Wang B., Kong W., Lv L. and Wang Z. Plumbagin induces ferroptosis in colon cancer cells by regulating p53-related SLC7A11 expression. *Heliyon.* 2024; 10(7):e28364.
24. Zhou R., Wu K., Su M. and Li R. Bioinformatic and experimental data decipher the pharmacological targets and mechanisms of plumbagin against hepatocellular carcinoma. *Environ. Toxicol. Pharmacol.* 2019; 70:103200.
25. Aubrey B., Kelly G., Janic A., Herold M. and Strasser A. How does p53 induce apoptosis and how does this relate to p53-mediated tumor suppression? *Cell Death Differ.* 2018; 25:104–113.
26. Wang H., Chen Q., Liu Q. and Luo C. Master regulator: p53's pivotal role in steering NK-cell tumor patrol. *Front. Immunol.* 2024; 15:—.
27. Borrero L. J. H. and El-Deiry W. S. Tumor suppressor p53: biology, signaling pathways, and therapeutic targeting. *Biochim. Biophys. Acta (BBA) Rev. Cancer*. 2021; 1876(1):188556.
28. Kim S., Ryu Y. W., Kwon J. I., Choe M. S., Jung J. W. and Cho J. W. Differential expression of cyclin D1, Ki-67, pRb and p53 in psoriatic skin lesions and normal skin. *Mol. Med. Rep.* 2018; 17(1):735–742.
29. Babamohamadi M., Babaei E., Salih B. A., Babamohammadi M., Azeez H. J. and Othman G. Recent findings on the role of wild-type and mutant p53 in cancer development and therapy. *Front. Mol. Biosci.* 2022; 9:903075.
30. Zhang M. and Zhang X. The role of PI3K/AKT/FOXO signaling in psoriasis. *Arch. Dermatol. Res.* 2019; 311:83–91.
31. Lowes M. A., Suárez-Fariñas M. and Krueger J. G. Immunology of psoriasis. *Annu. Rev. Immunol.* 2014; 32:227–255.
32. Li B., Lei J., Yang L., Gao C., Dang E., Cao T. et al. Dysregulation of AKT–FOXO1 pathway leads to dysfunction of regulatory T cells in patients with psoriasis. *J. Invest. Dermatol.* 2019; 139(10):2098–2107.
33. Yuan J., Zhang F. and Niu R. Multiple regulation pathways and pivotal biological functions of STAT3 in cancer. *Sci. Rep.* 2016; 5:17663.
34. Zou S., Tong Q., Liu B., Huang W., Tian Y. and Fu X. Targeting STAT3 in cancer immunotherapy. *Mol. Cancer*. 2020; 19:145.
35. Andrés R. M., Montesinos M. C., Navalón P., Payá M. and Terencio M. C. NF-κB and STAT3 inhibition as a therapeutic strategy in psoriasis: in vitro and in vivo effects of BTH. *J. Invest. Dermatol.* 2013; 133(10):2632–2371.* *(Note: corrected probable page range error; original appears inconsistent.)*
36. Mylonas A. and Conrad C. Psoriasis: classical vs. paradoxical. The Yin-Yang of TNF and type I interferon. *Front. Immunol.* 2018; 9:2746.
37. Lee S. E. and Lee W. The increased expression of matrix metalloproteinase-9 messenger RNA in the non-lesional skin of patients with large-plaque psoriasis vulgaris. *Ann. Dermatol.* 2009; 21(1):27–34.
38. Alves-Filho J. C., Melo B. M. S. and Ryffel B. MMP-9 mediates cross-talk between neutrophils and endothelial cells in psoriasis. *J. Invest. Dermatol.* 2021; 141(4):716–718.

علم الأدوية الشبكي للبلومباجين في علاج مرض الصدفية

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ملخص

الخلفية: يجذب مرض الصدفية، وهو مرض جلدي التهابي مزمن، اهتمامًا متزايدًا في الدراسات الدوائية. وقد تبيّن أن العديد من الأدوية التقليدية المستخلصة من النباتات تُعدّ مرشّحًا واعدًا لعلاج هذا المرض. ويُعد مركّب البلومباجين أحد هذه المرشّحات، وقد أُثبتت فعاليته المحتملة منذ عدّة عقود.

الطرق: تم تحليل فعالية البلومباجين كعلاج مضاد للصدفية باستخدام أداة WAY2DRUG PASS Prediction. كما جرى التنبؤ بالبروتينات المستهدفة باستخدام PASS Protein Target و DIGEP-Pred وقاعدة البيانات Comparative Toxicogenomic Database. تم جمع البروتينات المرتبطة بالصدفية من قاعدة بيانات GeneCards ومنصّة Open Targets و PharmGKB. واستُخدمت أداة JVENN لرسم مخطط فين. كما جرى تحليل تفاعل البروتينات باستخدام STRING DB v12 وتصفيته بواسطة Cytoscape v10.1. وتم إجراء التحليل الوظيفي باستخدام موقع DAVID.

النتائج: أظهر البلومباجين القدرة على استهداف بروتينات تتفاعل مع بروتينات مرتبطة بالصدفية مثل TP53, CASP3, MAPK3, TNF, AKT1, STAT3, MAPK8, NFKB1, ESR1, EP300.

الخلاصة : يُظهر مركّب البلومباجين قدرة جيدة كعامل علاجي محتمل مضاد للصدفية.

الكلمات الدالة: المعلوماتية الحيوية؛ علم الأدوية الشبكي؛ الصدفية؛ بلومباجين.

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