EJMA

DOI: 10.14744/ejma.2024.96168
EJMA 2024;4(4):177–183

Review

Unlocking the Biological Importance and Therapeutic Insights of Kuraridin: A Bioactive Prenylated Flavonoid from the Genus Sophora

Dinesh Kumar Patel, Kanika Patel

Department of Pharmaceutical Sciences, Sam Higginbottom University of Agriculture, Technology and Sciences, Prayagraj, Uttar Pradesh, India

Abstract

Prenylated flavonoids are one of the main active ingredients of Sophora species which have significant biological properties. Kuraridin, is a naturally occurring flavonoid in the roots of *Sophora flavescens* and possesses glycosidase inhibition, antibacterial, diacylglycerol acyltransferase, and tyrosinase inhibition activities. The present study summarized the scientific progress on the medical importance and pharmacological activity of kuraridin. Present review investigated the scientific research evidence of kuraridin available on various scientific databases such as PubMed, Springer, Google, Google Scholar, and Science Direct using the terms kuraridin, herbal medicine, *Sophora flavescens* and phytochemical. Present review described the medicinal importance and pharmacological activities of kuraridin in medicine. Analysis of scientific data signified the therapeutic potential of kuraridin against reovirus, gastric adenocarcinoma, tyrosine phosphatase 1B, antioxidant, BACE1 and cholinesterases, diacylglycerol acyltransferase, aldose reductase, inflammatory response, microorganism, enzymes and BKCa channel. Further present review also described the metabolomics and pharmacokinetic properties of kuraridin. Present review highlighted the biological potential of kuraridin in medicine.

Keywords: Kuraridin, medicine, *Sophora flavescens*, pharmacological, analytical, phytochemical

Cite This Article: *Patel DK, Patel K. Unlocking the Biological Importance and Therapeutic Insights of Kuraridin: A Bioactive Prenylated Flavonoid from the Genus Sophora. EJMA 2024;4(4):177–183.*

Medicinal plants and plant-derived by-products have been used as a source of food and medicines to treat human diseases for centuries, from ancient times to the present, in both developed and developing countries. Medicinal plants have many potential pharmacological and biological actions in medicine.[1–5] In Asian countries, traditional herbal medicine is used to treat human disorders and associated complications, and is still the most popular form of complementary and alternative medicine. Herbal medicine consists of various types of herbs and their derived by-products.[6–8] In addition, herbal medicines have also attracted attention in modern medicine.Plant secondary metabolites play important roles in plant growth and development.[9,10] The chemical diversity of phytochemicals has encouraged scientists to develop new types of medicines for human diseases in the modern medical era. The development of different colors, flavors, and order in plants is also believed to be due to the presence of these phytochemicals.[11–14] Plant-derived products have been utilized in the medicine, nutraceuticals, perfumery, beverages and cosmetics industries for different purpose.[15] Alkaloids, flavonoids, tannins, terpenoids and phenolic components are

Address for correspondence: Dinesh Kumar Patel, PhD. Department of Pharmaceutical Sciences, Sam Higginbottom University of Agriculture, Technology and Sciences, Prayagraj, Uttar Pradesh, India
Phone: +91-9919192440 **E-mail:** dkp.itbhu@gmail.com

Submitted Date: November 14, 2024 **Revision Date:** November 14, 2024 **Accepted Date:** November 28, 2024 **Available Online Date:** December 23, 2024

the most important class of active phytochemicals derived from plants.[16,17] Plants and the herbal products derived from them have always been excellent sources of natural antioxidants and have been used to treat various forms of cancer, inflammation, autoimmune diseases and diabetes. [18] The phenolic and flavonoid components are beneficial in cancer, cardiovascular and neurodegenerative diseases. [19] Furthermore, a large number of medicines are derived from natural products, the best examples of which are vinblastine, morphine, vincristine, papaverine and ephedrine. [20] Flavonoids are natural phenolic compounds containing diphenylpropane (C6-C3-C6) skeleton which exist in vegetables, fruits, wine, and medicated plants. Flavonoids can be classified into different sub class based on their skeleton, including anthocyanidins, flavones, flavanones, flavanols, flavonols, and isoflavones.[21,22] Flavonoids have anti-inflammatory, anti-malarial, anti-microbial, anti-bacterial, anti-oxidant, antiallergic, antiplasmodial, anti-cancer, anti-fungal, and neuroprotective activities.[23,24] The genus Sophora (Fabaceae) has been used in traditional medicine for years. Numerous class of prenylated flavonoids have been isolated from Sophora spp., including kuraridin (Fig. 1).[25] Prenylated flavonoids kuraridin has been isolated and characterized from the ethyl acetate fraction of the methanolic extract of *Albizzia julibrissin*.[26] The fingerprints of the flavonoids of Kushen Tang were established by HPLC under two detective wavelengths 280 nm and 365 nm in order to study its correlation to *Scutellaria baicalensis* and *Sophora flavescens*. Among them, eleven peaks, including peak for kuraridin were found to be present.[27]

An Overview of Kuraridin

Isoprenoid chalcones are the major flavonoids of *Sophora flavescens*. Kuraridin isolated from *Sophora flavescens* significantly reduced lipopolysaccharide (LPS)-induced reactive oxygen species (ROS) production, and suppressed the expression of inflammatory cytokines, tumor necrosis factor (TNF)-α, interleukin (IL)-1b, and Inducible nitric oxide synthase (iNOS) in LPS-stimulated RAW264.7 macrophages. Kuraridin inhibited TNFα-induced Nuclear factor-κB (NF-κB) transcriptional activity in HepG2 cells. Kuraridine exhibit glucosidase inhibition against β-glucosidase. Kuraridin also demonstrated noncompetitive inhibitions against protein tyrosine phosphatase 1B (PTP1B). Kuraridin are the predominant and abundant flavonoids in *Sophora flavescens*, and they are often selected as marker compounds in most quantitative studies.[28] The major components of the *Sophora flavescens* is kuraridin.[29] Kuraridin isolated from the roots of *Sophora flavescens* was found to inhibit eicosanoid producing enzymes such as cyclooxygenase-1 (COX-1), cyclooxygenase-2 (COX-2), 5-lipoxygenase (5-LOX) and 12-LOX.[30] Biological potential of kuraridin isolated from *Sophora flavescens* for their inhibitory potential on human type 1e3 reoviruses (HRV1e3) and Korean porcine reovirus (PRV) have been investigated in the scientific fields.[31] The cell-growth inhibitory effects of the mixture of kuraridin and nor-kurarinone has been investigated and examined their cytotoxic activity and mechanism using SGC-7901 cells.[32] Scientific study has revealed that prenylated flavonoids from *Sophora flavescens* exhibit a variety of bioactivities. Kuraridin displays a variety of biological activities, such as antitumor activity, PLCγ1 inhibitory activity, glycosidase inhibitory activity, SGLT inhibitory activity, tyrosinase inhibitory activity, antibacterial actions and anti-reovirus activity.[33] Kuraridin isolated from dichloromethane fraction of the ethanolic extract of *Sophora flavescens* showed tyrosinase inhibitory potential.[34] Bioactivity-guided fraction of an extract of *Sophora flavescens* led to the isolation of two new compounds, and 18 known flavonoids, including kuraridin.[35]

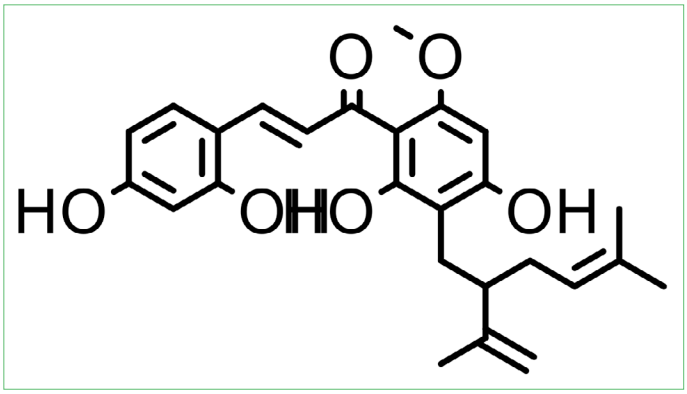

Figure 1. Chemical structure of kuraridin.

Pharmacological Activity of Kuraridin

Anti-Reovirus

Biological potential of kuraridin isolated from the roots of *Sophora flavescens* has been investigated for their anti-reovirus activity. No significant antiviral activity of kuraridin was detected in the pre-treatment assay. Further, of kuraridin were found to be 15.3-176.9 μM against human type 1-3 reoviruses (HRV1-3) and Korean porcine reovirus (PRV). Kuraridin completely blocked binding of viral sigma 1 protein to sialic acids at concentrations lower than 82.5 μM in the hemagglutination inhibition assay. Moreover, kuraridin inhibited HRV1-3 and PRV viral replication with EC_{50} values of 14.0-62.0 μM. The viral yields of kuraridin treated cells were significantly reduced at 24 h post-infection, compared with dimethyl sulfoxide (DMSO)-treated cells. Kuraridin inhibited virus adsorption and replication by inhibiting hemagglutination, viral ribonucleic acid (RNA) and protein synthesis and virus shedding.[31]

Gastric Adenocarcinoma

Molecular mechanisms of the mixture of compounds kuraridin and nor-kurarinone-induced growth inhibition including apoptosis and G2/M phase arrest in human gastric adenocarcinoma SGC-7901 cells have been investigated. Triggering of the mitochondrial apoptotic pathway was demonstrated by loss of mitochondrial membrane potential, reduction in the Bcl-2/Bax ratio, and significant activation and cleavage of caspase-3. Cytotoxic potential of the mixture of kuraridin and nor-kurarinone is mainly due to induction of cell cycle arrest and apoptosis.[32]

Tyrosine Phosphatase 1B

Five lavandulyl flavonoids, including kuraridin were isolated from the roots of *Sophora flavescens*, as novel PTP1B inhibitors. Kuraridin (IC_{50} <30μM) demonstrated to be noncompetitive inhibitors of protein tyrosine phosphatase 1B and exhibited different inhibitory selectivities against four homologous protein tyrosine phosphatases (T cell protein tyrosine phosphatase, vaccinia H1-related phosphatase, and Src homology domain 2-containing protein tyrosine phosphatases 1 and 2). Kuraridin also exhibited cellular activity in the insulin signaling pathway by increasing the insulin-stimulated Akt phosphorylation level in human hepatocellular liver carcinoma HepG2 cells.[36] *Sophora flavescens* was evaluated for tyrosinase inhibitory activity and its active principles were identified following activity-guided isolation. From the dichloromethane fraction, kuraridin was isolated. Compared with kojic acid, kuraridin possessed more potent tyrosinase inhibitory activity. The IC_{50} values was found to be 0.6 microM for kuraridin respectively.[37] Prenylated flavonoids containing the resorcinol moiety were isolated as tyrosinase inhibitors from the roots of *Sophora flavescens* by activity-guided fractionation. Among the 12 compounds isolated, kuraridin showed stronger inhibitory potencies (IC_{50} = 1.1, microM, respectively) than that of kojic acid (IC_{50} = 11.3 microM).[38]

Antioxidant

The antioxidant effects of the prenylated flavonoids from *Sophora flavescens* have been evaluated via in vitro 1,1-diphenyl-2-picrylhydrazyl (DPPH), 2,2'-azino-bis-3-ethylbenzothiazoline-6-sulfonic acid (ABTS), peroxynitrite (ONOO(-)), and total reactive oxygen species (ROS) assays. Kuraridin solated from *Sophora flavescens* was found to be a good DPPH scavengers.[39] Activity-guided fractionation of the CH_2Cl_2-soluble fraction of the roots of *Sophora flavescens* furnished five DPPH free radical scavengers. Other compounds exhibited significant DPPH free radical scavenging effects but not the kuraridin.[40]

BACE1 and Cholinesterases

Biological potential of lavandulylated flavanones from *Sophora flavescens* on beta-site APP cleaving enzyme 1 (BACE1) have been investigated. Beta-site APP cleaving enzyme 1 (BACE1) activities were significantly inhibited by kuraridin (IC_{50} 6.03 microM). Further, the prenyl group, rather than the lavandulyl group, and the flavonols and chalcones, rather than flavanones, might make predominant contributions to BACE1 inhibition. Therefore, *Sophora flavescens* and its prenylated flavonoids could be preventive and therapeutic candidates for Alzheimer's disease.[41]

Diacylglycerol Acyltransferase

Biological potential of four prenylflavonoids, including kuraridin isolated from the roots of *Sophora flavescens* were investigated for their inhibitory effects on diacylglycerol acyltransferase (DGAT). The flavonoids inhibited DGAT activity in a dose-dependent manner with IC_{50} values of 9.8 microM. The prenylflavonoids without C3-OH, including kuraridin showed stronger inhibition than those with C3-OH.[42]

Aldose Reductase

Biological potential of prenylated flavonoids isolated from *Sophora flavescens*, for their inhibitory activities on rat lens aldose reductase (AR) (RLAR), human recombinant AR (HRAR) and AGE formation have been investigated. Kuraridin showed significant inhibitory activities with IC_{50} 0.27 microM compared to the epalrestat. Thus, *Sophora flavescens* and its prenylated flavonoids posses potential for diabetic complications and related diseases.[43]

Inflammatory Response

Biological effects of kuraridin on COX-2 induction from RAW 264.7 cells and *in vivo* inflammatory response were studied. Prenylated flavonoids, including kuraridin down-regulated COX-2 induction at 10-25 uM.[44] Kuraridin inhibited inducible nitric oxide synthase (iNOS)-dependent nitric oxide (NO) production and ROS generation, and suppressed remarkably the expression of inflammatory cytokines, (TNF)-alpha, (IL)-1beta, and iNOS in LPS-stimulated RAW264.7 macrophages. Moreover kuraridin attenuated NF-kappaB activation by inhibition of IkappaBalpha proteolysis and p65 nuclear translocation, as well as phosphorylation of extracellular signal-regulated kinase (ERK)1/2, c-Jun N-terminal kinase (JNK), and p38 MAP kinases.[45]

Microorganism

Antimicrobial activity of the 18 prenylated flavonoids purified from five different medicinal plants was evaluated by determination of MIC using the broth microdilution methods against four bacterial and two fungal microorganisms (*Candida albicans, Saccaromyces cerevisiae, Escherichia coli, Salmonella typhimurium, Staphylococcus epidermis* and *Staphylococcus aureus*). Kuraridin exhibited a good antifungal activity with strong antibacterial activity.[46] Antibacterial activities of different phytochemicals of *Sophora flave-*

scens have been investigated. Kuraridin was isolated from the best anti-methicillin-resistant *Staphylococcus aureus* (MRSA) fraction. Kuraridin exhibited significant anti-MRSA effects, compared to baicalein. Further, kuraridin showed no toxicity on human peripheral blood mononuclear cells (PBMC) at the concentration up to 64 µg/ml.[47]

Enzymes

Biological effects of 19 naturally occurring prenylated flavonoids, isolated from medicinal plants, on COX-1 and COX-2 and on 5-LOX and 12-LOX were investigated using [14C] arachidonic acid as a substrate. Kuraridin inhibited COX-1 activity. Kuraridin is having a C-8 lavandulyl moiety and showed potent activity IC_{50} = 0.1 to 1 microM compared to that of indomethacin IC_{50} = 0.7 microM.[48] The methanol extract of *Sophora flavescens* showed a potent glycosidase inhibitory activity. Biological potential of active components of of *Sophora flavescens* were identified for their alpha-glucosidase inhibitory potential. All flavonoids were effective inhibitors of alpha-glucosidase and beta-amylase. Kuraridine exhibited IC_{50} value of 57 microM against beta-glucosidase. Further, the inhibition pattern was noncompetitive for alpha-glucosidase, whereas mixed inhibition was observed for beta-amylase.[49]

BKCa Channel

Biological potential of flavonoid components isolated from *Sophora flavescens* have been evaluated for its effectiveness on BKCa channel. Among the 13 compounds tested, six flavonoids were found to activate the Ca^{2+}-activated K^+ (BKCa) channel and kuraridin is a new activators of the BKCa channel.[50]

Metabolomics

A novel integrated strategy combining metabolomics and network pharmacology was developed to explore the quality markers from *Sophora flavescens*. The targeted metabolomic profiles of seventy-four batches of *Sophora flavescens* (aged from 1 to 6 years) has been determined by ultra-high-performance liquid chromatography coupled with high-field quadrupole-orbitrap mass spectrometry (UHPLC-QE-MS). The anti-tumor activity of six flavonoids, including kuraridin as the quality markers for *Sophora flavescens* were determined and also evaluated their pharmacokinetic profiles.[51] Pharmacodynamic effects of the ethyl acetate extract of *Sophora flavescens* against dextran sodium sulfate-induced ulcerative colitis (UC) rats have been investigated. A total of 28 prototypes and 41 metabolites were unambiguously or tentatively detected in rat's plasma and urine, and mong them, kuraridin was suggested to be potential active compounds in *Sophora flavescens* for treating UC by comprehensively investigating the results of network pharmacology analysis, metabolic analysis *in vivo*, and previous researches.[52]

Pharmacokinetics

An ultra-performance liquid chromatography/tandem mass spectrometry (UHPLC-MS/MS) method has been developed for the quantification and characterization metabolites in rat plasma after oral administration of kuraridin. A liquid-liquid extraction method with ethyl acetate-acetonitrile (1:3) was used to extract the kuraridin from rat plasma samples. The chromatographic separation was carried out on a Hypersil GOLD UHPLC C18 column equipped with a C18 guard cartridge using a gradient elution with organic solvent-water as mobile phase. Under the optimized conditions, the method showed good linearity ($r^2 > 0.99$) over the ranges of 1-500 ng/mL for kuraridin. The developed UHPLC-MS/MS method was successfully applied in the quantitative analysis of kuraridin in rat plasma.[33]

Conclusion

Present review described the biological potential and pharmacological activities of kuraridin through scientific data analysis of different research work of kuraridin. For the present review, we have collected all the scientific information of kuraridin from PubMed, Springer, Google, Google Scholar and Science Direct and analyzed here in order to know their therapeutic potential in medicine. Present review summarized the pharmacological activities of kuraridin and provided a reference for future studies focused on biological applications of kuraridin in medicine. Present review revealed the therapeutic importance of kuraridin in medicine. Analysis of collected scientific data signified the biological potential of kuraridin against reovirus, gastric adenocarcinoma, tyrosine phosphatase 1B, antioxidant, BACE1 and cholinesterases, diacylglycerol acyltransferase, aldose reductase, inflammatory response, microorganism, enzymes and BKCa channel. Further present review also described their metabolomics and pharmacokinetic properties (Fig. 2). Present review will be beneficial for all the scientific researchers to know the health

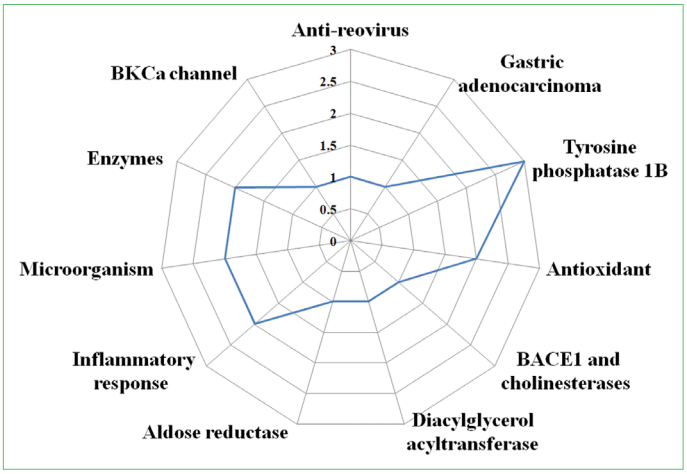

Figure 2. Biological potential of kuraridin.

beneficial aspects of kuraridin in medicine. Scientific data analysis revealed the presence of kuraridin in *Sophora flavescens*. Moreover, scientific research needs to be conducted to get more scientific information about the presence of kuraridin in other natural sources. Kuraridin have many biological activities in medicine, but their therapeutic effectiveness against other related secondary complications in humans is also investigated in the scientific field in order to know their therapeutic effects in modern medicine. There is also a need to explore and develop new and advanced analytical methods for the isolation and quantification of kuraridin in different biological and non-biological samples.

Disclosures

Acknowledgments: The authors want to acknowledge Sam Higginbottom University of Agriculture, Technology and Sciences, Prayagraj, Uttar Pradesh, India for online article support.

Funding: None.

Peer-review: Externally peer-reviewed.

Conflict of Interest: The authors report no conflict of interest.

Authorship Contributions: Concept – D.K.P.; Design – D.K.P.; Supervision – D.K.P.; Materials – D.K.P., K.P.; Data collection and/or processing – D.K.P., K.P.; Analysis and/or interpretation – D.K.P.; Literature search – D.K.P., K.P.; Writing – D.K.P., K.P.; Critical review – D.K.P., K.P.

References

1. Patel K, Patel DK. Biological importance and therapeutic effectiveness of thaliporphine in medicine: An aporphine alkaloid from natural sources. Pharmacol Res Nat Prod 2024;2:100019..
2. Patel DK. Biological importance and therapeutic potential of trilobatin in the management of human disorders and associated secondary complications. Pharmacol Res Mod Chinese Med 2022;5:100185.
3. Patel DK. Therapeutic role of columbianadin in human disorders: Medicinal importance, biological properties and analytical aspects. Pharmacol Res Mod Chinese Med 2023;6:100212.
4. Patel K, Patel DK. Therapeutic significance of cornin in medicine for their biological importance and pharmacological activity: An overview of iridoid glycosides of verbena officinalis L. Curr Funct Foods 2024;3:e260124226402.
5. Patel DK, Patel K. Biological importance and therapeutic potential of calycopterin from dracocephalum kotschyi: An overview of current scientific research work. Recent Adv Anti-Infective Drug Discov 2024;19:12–20.
6. Patel DK. Grandisin and its therapeutic potential and pharmacological activities: A review. Pharmacol Res Mod Chinese Med 2022;5:100176.
7. Patel DK. Therapeutic effectiveness of magnolin on cancers and other human complications. Pharmacol Res Mod Chinese Med 2023;6:100203.
8. Patel DK. Biological importance of a biflavonoid 'bilobetin' in the medicine: medicinal importance, pharmacological activities and analytical aspects. Infect Disord Drug Targets 2022;22:e210322202490.
9. Patel K, Patel DK. Biological potential and therapeutic effectiveness of pteryxin in medicine. A viable alternative to current remedies for the treatment of human disorders. Pharmacol Res Mod Chinese Med 2024;10:100405.
10. Patel DK. Biological potential and therapeutic benefit of chrysosplenetin: An applications of polymethoxylated flavonoid in medicine from natural sources. Pharmacol Res Mod Chinese Med 2022;4:100155.
11. Patel DK. Biological importance of bioactive phytochemical 'Cimifugin' as potential active pharmaceutical ingredients against human disorders: A natural phytochemical for new therapeutic alternatives. Pharmacol Res Mod Chinese Med 2023;7:100232.
12. Patel DK, Patel K. Potential therapeutic applications of eudesmin in medicine: An overview on medicinal importance, pharmacological activities and analytical prospects. Pharmacol Res Mod Chinese Med 2022;5:100175.
13. Patel K, Patel DK. Secoiridoid amarogentin from 'gentianaceae' with their health promotion, disease prevention and modern analytical aspects. Curr Bioact Compd 2020;16:191–200.
14. Patel K, Patel DK. Health benefits of avicularin in the medicine against cancerous disorders and other complications: Biological importance, therapeutic benefit and analytical aspects. Curr Cancer Ther Rev 2022;18:41–50.
15. Patel DK. Health benefits, therapeutic applications, and recent advances of cirsilineol in the medicine: Potential bioactive natural flavonoids of genus artemisia. Endocr Metab Immune Disord Drug Targets 2023;23:894–907.
16. Patel K, Patel DK. Biological importance, pharmacological activities, and nutraceutical potential of capsanthin: A Review of capsicum plant capsaicinoids. Curr Drug Res Rev 2024;16:18–31.
17. Patel DK, Patel K. Herbal medicines genkwadaphnin as therapeutic agent for cancers and other human disorders: A Review of pharmacological activities through scientific evidence. Curr Tradit Med 2024;10:e230523217251.
18. Patel DK, Patel K. An overview of medicinal importance, pharmacological activities and analytical aspects of fraxin from cortex fraxinus. Curr Tradit Med 2023;9:109–115.
19. Patel DK. Biological importance, therapeutic benefit, and medicinal importance of flavonoid, cirsiliol for the development of remedies against human disorders. Curr Bioact Compd 2022;18:e240821195804.
20. Patel K, Patel DK. Therapeutic benefit and biological importance of ginkgetin in the medicine: Medicinal importance, pharmacological activities and analytical aspects. Curr Bioact Compd 2021;17:e190721190770.
21. Patel DK, Patel K. Biological potential of aromadendrin against

human disorders: Recent development in pharmacological activities and analytical aspects. Pharmacol Res Mod Chinese Med 2024;11:100424.
22. Patel DK. Medicinal importance, pharmacological activities, and analytical aspects of engeletin in medicine: Therapeutic benefit through scientific data analysis. Endocr Metab Immune Disord Drug Targets 2023;23:273–282.
23. Patel K, Patel DK. Medicinal importance and therapeutic benefit of bioactive flavonoid eriocitrin: An update on pharmacological activity and analytical aspects. Nat Prod J 2024;14:e100723218583.
24. Patel DK. Biological Importance, therapeutic benefits, and analytical aspects of active flavonoidal compounds 'corylin' from psoralea corylifolia in the field of medicine. Infect Disord Drug Targets 2023;23:e250822208005.
25. Boozari M, Soltani S, Iranshahi M. Biologically active prenylated flavonoids from the genus sophora and their structure-activity relationship - A review. Phyther Res 2019;33:546–560.
26. Jung MJ, Kang SS, Jung HA, Kim GJ, Choi JS. Isolation of flavonoids and a cerebroside from the stem bark of albizzia julibrissin. Arch Pharm Res 2004;27:593.
27. Liu B, Shi RB, Zhu LJ. HPLC fingerprint of flavonoids of kushen tang and its correlation to scutellaria baicalensis and sophora flavescens. Zhongguo Zhongyao Zazhi 2007;32:1631–4.
28. Li J, Zhang X, Shen X, Long Q, Xu C, Tan C, et al. Phytochemistry and biological properties of isoprenoid flavonoids from Sophora flavescens Ait. Fitoterapia 2020;143:104556.
29. Chong E, Hwang GB, Nho CW, Kwon BM, Lee JE, Seo S, et al. Antimicrobial durability of air filters coated with airborne Sophora flavescens nanoparticles. Sci Total Environ 2013;444:110–114.
30. Jin JH, Kim JS, Kang SS, Son KH, Chang HW, Kim HP. Anti-inflammatory and anti-arthritic activity of total flavonoids of the roots of Sophora flavescens. J Ethnopharmacol 2010;127:589–595.
31. Kwon HJ, Jeong JH, Lee SW, Ryu YB, Jeong HJ, Jung K, et al. In vitro anti-reovirus activity of kuraridin isolated from sophora flavescens against viral replication and hemagglutination. J Pharmacol Sci 2015;128:159–169.
32. Rasul A, Yu B, Yang LF, Ali M, Khan M, Ma T, et al. Induction of mitochondria-mediated apoptosis in human gastric adenocarcinoma SGC-7901 cells by kuraridin and nor-kurarinone isolated from sophora flavescens. Asian Pacific J Cancer Prev 2011;12:2499–504.
33. Liu Y, Chen L, Cai W, Zhao L, Mo Z. Use of an UHPLC-MS/MS method for determination of kuraridin and characterization of its metabolites in rat plasma after oral administration. Molecules 2018;23:132.
34. Hyun SK, Lee WH, Jeong DM, Kim Y, Choi JS. Inhibitory effects of kurarinol, kuraridinol, and trifolirhizin from sophora flavescens on tyrosinase and melanin synthesis. Biol Pharm Bull 2008;31:154–158.
35. Li P, Chai WC, Wang ZY, Tang KJ, Chen JY, Venter H, et al. Bioactivity-guided isolation of compounds from sophora flavescens with antibacterial activity against acinetobacter baumannii. Nat Prod Res 2022;36:4334–4342.
36. Sasaki T, Li W, Higai K, Quang TH, Kim YH, Koike K. Protein tyrosine phosphatase 1B inhibitory activity of lavandulyl flavonoids from roots of Sophora flavescens. Planta Med 2014;80:557–560.
37. Kim SJ, Son KH, Chang HW, Kang SS, Kim HP. Tyrosinase inhibitory prenylated flavonoids from sophora flavescens. Biol Pharm Bull 2003;26:1348–1350.
38. Son JK, Park JS, Kim JA, Kim Y, Chung SR, Lee SH. Prenylated flavonoids from the roots of sophora flavescens with tyrosinase inhibitory activity. Planta Med 2003;69:559–561.
39. Jung HA, Jeong DM, Chung HY, Lim HA, Kim JY, Yoon NY, et al. Re-evaluation of the antioxidant prenylated flavonoids from the roots of sophora flavescens. Biol Pharm Bull 2008;31:908–15.
40. Jung HJ, Kang SS, Hyun SK, Choi JS. In vitro free radical and ONOO- Scavengers from sophora flavescens. Arch Pharm Res 2005;28:534–540.
41. Jung HA, Yokozawa T, Kim BW, Jung JH, Choi JS. Selective inhibition of prenylated flavonoids from sophora flavescens against BACE1 and cholinesterases. Am J Chin Med 2010;38:415–429.
42. Chung MY, Rho MC, Ko JS, Ryu SY, Jeune KH, Kim K, et al. In vitro Inhibition of Diacylglycerol Acyltransferase by Prenylflavonoids from Sophora flavescens. Planta Med 2004;70:258–260.
43. Jung HA, Yoon NY, Kang SS, Kim YS, Choi JS. Inhibitory activities of prenylated flavonoids from Sophora flavescens against aldose reductase and generation of advanced glycation end-products. J Pharm Pharmacol 2010;60:1227–1236.
44. Kim DW, Chi YS, Son KH, Chang HW, Kim JS, Kang SS, et al. Effects of sophoraflavanone g, a prenylated flavonoid from sophora Flavescens, on cyclooxygenase-2 and In vivo inflammatory response. Arch Pharm Res 2002;25:329–335.
45. Han JM, Jin YY, Kim HY, Park KH, Lee WS, Jeong TS. Lavandulyl flavonoids from sophora flavescens suppress lipopolysaccharide-induced activation of nuclear factor-κB and mitogen-activated protein kinases in RAW264.7 cells. Biol Pharm Bull 2010;33:1019-23.
46. Sohn HY, Son KH, Kwon CS, Kwon GS, Kang SS. Antimicrobial and cytotoxic activity of 18 prenylated flavonoids isolated from medicinal plants: Morus alba L., morus mongolica schneider, broussnetia papyrifera (L.) vent, sophora flavescens ait and echinosophora koreensis nakai. Phytomedicine 2004;11:666–672.
47. Chan BCL, Yu H, Wong CW, Lui SL, Jolivalt C, Ganem-Elbaz C, et al. Quick identification of kuraridin, a noncytotoxic anti-MRSA (methicillin-resistant Staphylococcus aureus) agent from so-

phora flavescens using high-speed counter-current chromatography. J Chromatogr B 2012;880:157–162.
48. Chi YS, Jong HG, Son KH, Chang HW, Kang SS, Kim HP. Effects of naturally occurring prenylated flavonoids on enzymes metabolizing arachidonic acid: Cyclooxygenases and lipoxygenases. Biochem Pharmacol 2001;62:1185-91.
49. Kim JH, Ryu YB, Kang NS, Lee BW, Heo JS, Jeong IY, et al. Glycosidase inhibitory flavonoids from sophora flavescens. Biol Pharm Bull 2006;29:302–305.
50. Lee S, Choi JS, Park CS. Direct activation of the largeconductance calcium-activated potassium channel by flavonoids isolated from sophora flavescens. Biol Pharm Bull 2018; 41:1295–1298.
51. Chen L, Huang X, Wang H, Shao J, Luo Y, Zhao K, et al. Integrated metabolomics and network pharmacology strategy for ascertaining the quality marker of flavonoids for Sophora flavescens. J Pharm Biomed Anal 2020;186:113297.
52. Chen L, Shao J, Luo Y, Zhao L, Zhao K, Gao Y, et al. An integrated metabolism in vivo analysis and network pharmacology in UC rats reveal anti-ulcerative colitis effects from Sophora flavescens EtOAc extract. J Pharm Biomed Anal 2020;186:113306.