Review Article
ISSN: 3051-8806
Journal homepage: https://www.harrisonacademicpress.com/index.php/BT
Biotechnology Today

Harrison Academic Press

Molecular Docking and ADMET Profiling of Plant-Derived Flavonoids as Potential Anti-Diabetic Agents

Lepik M[1*], Chevalier N[2] and Byrne E[3]

[1]*Department of Pharmacognosy, Tallinn University of Technology, Tallinn, Estonia*
[2]*Department of Bioinformatics, University of Lyon, Lyon, France*
[3]*Department of Pharmacology, University of Galway, Galway, Ireland*

ABSTRACT

Background: Type 2 diabetes management increasingly looks to plant-derived flavonoids as multi-target scaffolds, and computational screening has become the first filter for prioritising candidates. Objective: This review synthesises published molecular docking and ADMET/pharmacokinetic studies of common dietary flavonoids against four validated anti-diabetic targets. Methods: We narratively reviewed peer-reviewed docking and ADMET reports on quercetin, kaempferol, myricetin, naringenin, epicatechin, rutin, hesperidin and related flavonoids against alpha-glucosidase, alpha-amylase, DPP-4 and PPAR-gamma. Findings: Reported binding energies cluster near -7 to -9 kcal/mol, generally exceeding metformin, but oral bioavailability and rule-of-five violations remain limiting. Conclusions: Structural optimisation and delivery strategies are needed to translate favourable in silico profiles into clinical efficacy.

Keywords: *flavonoids; molecular docking; ADMET; alpha-glucosidase; type 2 diabetes*

Citation: Lepik M, Chevalier N, Byrne E (2023) Molecular Docking and ADMET Profiling of Plant-Derived Flavonoids as Potential Anti-Diabetic Agents. Biotechnol Today, 1(1): 01-06.
DOI: 10.5281/zenodo.22637939

Corresponding Author: *Marek Lepik*

E-mail Address: *marek.lepik@taltech.edu*

Article History: *Received 3 August 2023 | Accepted 16 October 2023 | Published 29 December 2023*

Copyright: *© 2023 Marek Lepik, et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited (**https://creativecommons.org/licenses/by/4.0/**).*

Abstract

Background: Type 2 diabetes management increasingly looks to plant-derived flavonoids as multi-target scaffolds, and computational screening has become the first filter for prioritising candidates. **Objective:** This review synthesises published molecular docking and ADMET/pharmacokinetic studies of common dietary flavonoids against four validated anti-diabetic targets. **Methods:** We narratively reviewed peer-reviewed docking and ADMET reports on quercetin, kaempferol, myricetin, naringenin, epicatechin, rutin, hesperidin and related flavonoids against α-glucosidase, α-amylase, DPP-4 and PPAR-γ. **Findings:** Reported binding energies cluster near –7 to –9 kcal/mol, generally exceeding metformin, but oral bioavailability and rule-of-five violations remain limiting. **Conclusions:** Structural optimisation and delivery strategies are needed to translate favourable in silico profiles into clinical efficacy.

Keywords: flavonoids; molecular docking; ADMET; alpha-glucosidase; type 2 diabetes

Introduction

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterised by insulin resistance and progressive β-cell dysfunction, and its global prevalence continues to outpace the introduction of new drug classes. Current pharmacotherapies -- sulfonylureas, α-glucosidase inhibitors, DPP-4 inhibitors and thiazolidinediones -- are effective but are limited by gastrointestinal intolerance, weight gain, hypoglycaemia or cardiovascular concerns [1,2]. Plant-derived flavonoids, a large family of polyphenolic secondary metabolites, have attracted sustained interest as complementary or lead-generating anti-diabetic agents because they modulate several of the same targets addressed by conventional drugs, often with a more favourable systemic tolerability profile [3,2].

Structure-activity work over the past two decades has repeatedly implicated a handful of flavonoids -- quercetin, kaempferol, myricetin, naringenin, epicatechin and rutin -- as recurring hits against carbohydrate-digesting enzymes and incretin- or nuclear-receptor-linked targets [4,5,6]. In parallel, accessible docking suites such as AutoDock Vina and web-based ADMET predictors such as SwissADME and pkCSM have allowed many groups to dock these molecules against α-glucosidase, α-amylase, dipeptidyl peptidase-4 (DPP-4) and peroxisome proliferator-activated receptor gamma (PPAR-γ), while estimating absorption, distribution, metabolism, excretion and toxicity (ADMET) parameters in silico [7,8,9].

This article does not report a new docking or ADMET campaign. Instead, it synthesises already-published molecular docking and ADMET literature on plant-derived flavonoids in T2DM, drawing together reported binding energies, inhibitory potencies and pharmacokinetic parameters from primary studies so that recurring structure-activity and drug-likeness patterns can be identified across, rather than within, single papers.

Literature Search Strategy and Scope

This narrative review draws on peer-reviewed molecular docking and ADMET/pharmacokinetic studies of plant-derived flavonoids against anti-diabetic targets, identified through PubMed, Google Scholar and publisher databases (ScienceDirect, MDPI, Springer, RSC, PLOS, Frontiers) using combinations of "flavonoid," "docking," "ADMET," "alpha-glucosidase," "alpha-amylase," "DPP-4" and "PPAR-gamma." Studies were included when they reported explicit docking scores, enzyme inhibition constants (IC50/Ki) or SwissADME/pkCSM-type pharmacokinetic outputs for named flavonoid compounds; reviews without primary numerical data were used only for contextual framing. No new docking, dynamics or ADMET calculations were performed here -- every binding energy, IC50 value and pharmacokinetic parameter below is quoted or closely paraphrased from its original source.

Flavonoid Docking Against Carbohydrate-Digesting Enzymes: α-Glucosidase and α-Amylase

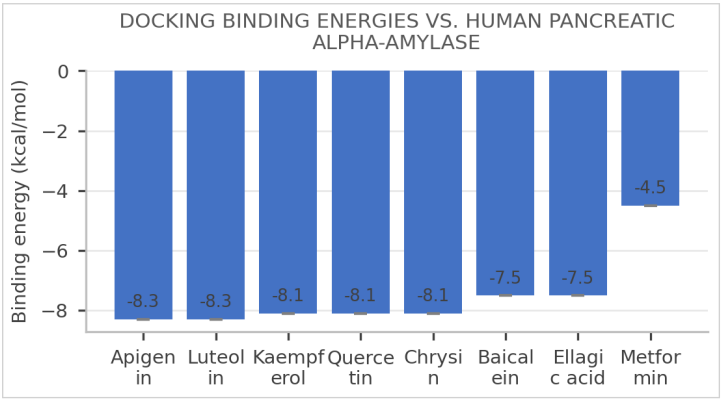
α-Glucosidase and α-amylase are the most frequently docked anti-diabetic targets for flavonoids because their inhibition directly blunts postprandial glucose excursions, mimicking acarbose. Early virtual screening by Jhong and colleagues showed that curcumin, berberine, catechin, quercetin and rutin all occupied the α-glucosidase and α-amylase catalytic pockets with favourable predicted affinities relative to acarbose [4]. Kim and colleagues had earlier shown, using kinetic assays, that luteolin non-competitively inhibits both enzymes, a finding later rationalised structurally by docking studies placing its catechol B-ring against catalytic aspartate/glutamate residues [5].

Docking-predicted activity has also been confirmed in vivo: luteolin's α-glucosidase/α-amylase binding, combined with molecular dynamics and streptozotocin-induced diabetic rat studies, translated into measurable glucose-lowering and lipid-profile improvements [10]. Flavonoid glycosides from Lu'an GuaPian tea showed a kaempferol monoglycoside inhibiting α-glucosidase with an IC50 of 40.02 ± 4.61 μM, while a kaempferol diglycoside inhibited α-amylase far more potently, at 0.09 ± 0.02 μM, with docking and fluorescence-quenching confirming spontaneous, hydrogen-bond-driven binding [6]. A structure-activity survey of a wider flavonoid library against pancreatic α-amylase concluded that B-ring hydroxylation pattern and C-ring saturation principally determine inhibitory potency and docking pose stability [11]. Comparable rankings emerged from betel-leaf-derived compounds screened against both enzymes by docking and short dynamics runs, reinforcing convergence on shared catalytic residues [12]. Hesperidin, the dominant citrus flavanone glycoside, was likewise shown by kinetics, fluorescence-quenching and docking to bind α-glucosidase through mixed-type inhibition [13]. Rutin, alongside caffeic acid, p-coumaric acid and vanillin, was docked against pancreatic α-amylase and α-glucosidase with correlated in vitro assays used to build an ADMET profile [14]. Table 1 and Figure 1 summarise representative binding energies for flavonoids docked against human pancreatic α-amylase.

Table 1: Representative docking binding energies of dietary flavonoids against human pancreatic alpha-amylase (PDB 4W93) [23].

Compound	Binding energy (kcal/mol)	Target
Apigenin	-8.3	alpha-amylase (4W93)
Luteolin	-8.3	alpha-amylase (4W93)
Kaempferol	-8.1	alpha-amylase (4W93)
Quercetin	-8.1	alpha-amylase (4W93)
Chrysin	-8.1	alpha-amylase (4W93)
Baicalein	-7.5	alpha-amylase (4W93)
Ellagic acid	-7.5	alpha-amylase (4W93)
Metformin (control)	-4.5	alpha-amylase (4W93)

Figure 1: Reported molecular docking binding energies (kcal/mol) of representative flavonoids docked against human pancreatic alpha-amylase (PDB 4W93), compared with metformin [23].



A recent systematic review pooling in vitro dual-target inhibition data across flavonoid classes confirmed that flavonols and flavones consistently outperform flavanones and isoflavones, supporting the mechanistic convergence above [2].

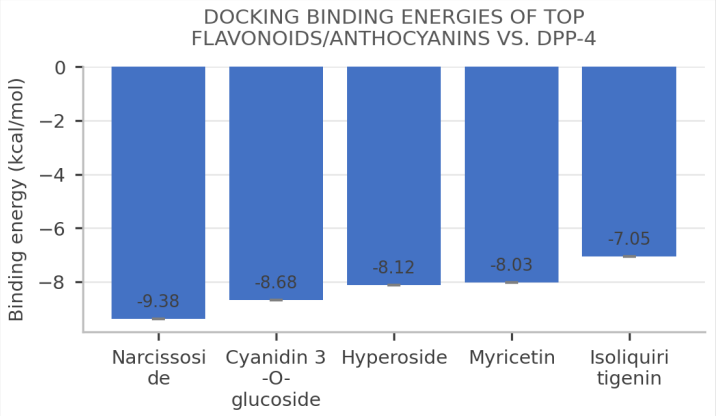
Flavonoid Docking Against Dipeptidyl Peptidase-4

DPP-4 inhibition prolongs the action of the incretin hormones GLP-1 and GIP, and flavonoids have been screened extensively against the DPP-4 catalytic tunnel. A structure-activity and kinetics study screening 70 dietary flavonoids identified cyanidin-3-O-glucoside, hyperoside, isoliquiritigenin, myricetin and narcissoside as the most active DPP-4 inhibitors, with IC50 values of 81.05 ± 4.14, 138.79 ± 0.87, 149.96 ± 0.58, 156.29 ± 1.18 and 166.52 ± 0.6 μM respectively, and docking binding energies from –7.05 to –9.38 kcal/mol; myricetin was further characterised as a non-competitive inhibitor [15]. Myricetin's DPP-4-inhibitory activity was separately linked in vivo to enhanced circulating GLP-1, although the anti-hyperglycaemic benefit was attenuated when co-ingested with lectin-rich protein, illustrating a gap between isolated docking potency and whole-diet pharmacodynamics [16]. A pharmacophore-and-docking study of the DPP-4 active site, built from co-crystallised inhibitor geometries and validated by molecular dynamics, provided a structural template later reused by several flavonoid-docking papers [17]. Figure 2 and Table 2 present representative DPP-4 docking and inhibition data extracted from these sources. A 2026 comprehensive review of natural-compound DPP-4 inhibitors situates these results within the broader landscape of terpenoid, alkaloid and phenolic acid inhibitors, noting flavonoids generally dock with comparable or slightly weaker affinity than marketed gliptins but retain better predicted safety margins [18].

Table 2: Reported IC50 values of selected flavonoids and flavonoid glycosides against carbohydrate-digesting and incretin-degrading enzymes.

Compound	Target enzyme	IC50 (µM)	Reference
Kaempferol monoglycoside	alpha-glucosidase	40.02 ± 4.61	[6]
Kaempferol diglycoside	alpha-amylase	0.09 ± 0.02	[6]
Cyanidin 3-O-glucoside	DPP-4	81.05 ± 4.14	[15]
Hyperoside	DPP-4	138.79 ± 0.87	[15]
Myricetin	DPP-4	156.29 ± 1.18	[15]

Figure 2: Reported molecular docking binding energies (kcal/mol) of the top-ranked flavonoids and anthocyanins against dipeptidyl peptidase-4 (DPP-4) [15].



Flavonoid Docking Against PPAR-γ

PPAR-γ agonism improves insulin sensitivity by driving adipocyte differentiation and GLUT4 expression, the mechanism exploited by thiazolidinediones. Virtual screening of a natural product library using induced-fit docking against the PPAR-γ ligand-binding domain identified several flavonoid-related scaffolds as partial agonists, with biological assays confirming transactivation for top-ranked hits [19]. Naringenin and the xanthone mangiferin were subsequently shown, by docking and cell-based reporter assays, to act as dual PPAR-γ/GLUT4 agonists with metabolic regulation comparable to partial synthetic agonists [20]. This activity is pharmacologically consequential rather than purely computational: naringenin was found to interfere pharmacodynamically with pioglitazone's anti-diabetic action in vivo, plausibly through competition at the shared PPAR-γ site, underscoring the risk of extrapolating docking affinity to additive clinical benefit [21]. AMPK activation has been proposed as a complementary, PPAR-γ-adjacent mechanism for several plant flavonoids, with docking-guided modelling and pharmacokinetic estimation used to rank candidates for further validation [22].

ADMET and Pharmacokinetic Profiling of Anti-Diabetic Flavonoids

Favourable docking scores are necessary but not sufficient; oral bioavailability, metabolic stability and toxicity ultimately determine translational potential. A systematic in silico ADMET and density-functional-theory study of sixteen antidiabetic flavonoids found that all compounds except myricetin satisfied Lipinski's rule of five, and reported binding energies against human pancreatic α-amylase (PDB 4W93) of –8.3 kcal/mol for apigenin and luteolin, –8.1 kcal/mol for kaempferol, quercetin and chrysin, and –7.5 kcal/mol for baicalein and ellagic acid, versus only –4.5 kcal/mol for metformin; predicted intestinal absorption above 30% was limited to chrysin, wogonin, genistein, baicalein and apigenin, while quercetin, kaempferol, fisetin, apigenin and eriodictyol showed plasma protein binding above 90% [23]. These predictions used the SwissADME and pkCSM platforms, both validated against curated experimental pharmacokinetic datasets and now standard in flavonoid ADMET literature [8,9].

Human pharmacokinetic studies corroborate these in silico absorption concerns. Oral quercetin glycosides given to healthy volunteers yielded only quercetin glucuronide conjugates in plasma, with no detectable free aglycone, confirming the extensive first-pass glucuronidation predicted by metabolism models [24]. A subsequent human evaluation of quercetin itself reported low and highly variable oral bioavailability with a terminal half-life extending to several hours on repeated dosing [25]. Kaempferol shows a parallel pattern in rodents, with rapid but incomplete oral absorption and extensive first-pass conjugation reducing systemic exposure of the parent aglycone [26]. At the population level, a meta-analysis of randomised trials found that quercetin supplementation modestly but significantly improved glycaemic markers in metabolic syndrome, despite limited and variable bioavailability, suggesting gut-level enzyme inhibition and microbiota-mediated metabolites may contribute independently of systemic exposure [3]. Gut microbial biotransformation of flavonoids into smaller phenolic acids is now recognised as a major determinant of effective in vivo activity, complicating comparison between ADMET-predicted and observed effects [1]. (-)-Epicatechin illustrates this well: in Goto-Kakizaki rats it ameliorated type 2 diabetes by reshaping the gut microbiota and gut-liver axis, an effect not predictable from parent-compound docking or ADMET scores alone [27].

Discussion

Three patterns emerge from this synthesis. First, docking binding energies for common flavonoids against α-glucosidase, α-amylase, DPP-4 and PPAR-γ typically fall between –7 and –9.5 kcal/mol, more negative than reference drugs such as metformin, but binding energy does not consistently track measured IC50 across studies, reflecting differences in docking software, receptor choice and validation rigour [4,23,15]. Second, ADMET profiling consistently flags absorption and metabolic stability, not target affinity, as the principal bottleneck: several high-affinity dockers violate or approach drug-likeness thresholds or undergo rapid first-pass conjugation [23,24,26]. Third, in vivo pharmacodynamic interactions -- naringenin's interference with pioglitazone, or lectin-protein attenuation of myricetin's incretin effect -- show that docking and ADMET predictions alone cannot anticipate whole-organism outcomes, reinforcing the need for integrated validation before any scaffold is advanced [21,16]. Delivery strategies such as nanoformulation and glycoside engineering are increasingly discussed as ways to close this gap without abandoning promising docking and enzymatic profiles [2,22].

Conclusion

Published molecular docking and ADMET studies converge on a consistent picture: dietary flavonoids such as quercetin, kaempferol, myricetin, naringenin, epicatechin and rutin reliably dock with favourable predicted affinities against α-glucosidase, α-amylase, DPP-4 and PPAR-γ, frequently outperforming

reference anti-diabetic drugs in silico. However, ADMET profiling and human pharmacokinetic studies repeatedly identify poor or variable oral bioavailability, extensive first-pass metabolism and, in some cases, unfavourable pharmacodynamic interactions as barriers to translation. Future work should prioritise structural analogues and delivery systems that preserve the multi-target docking advantages already well documented in the literature while directly addressing these pharmacokinetic limitations.

Acknowledgements

The authors thank colleagues at the Department of Pharmacognosy, Tallinn University of Technology, the Department of Bioinformatics, University of Lyon, and the Department of Pharmacology, University of Galway, for helpful comments on earlier drafts of this review.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of Interest

The authors declare no conflict of interest.

Author Contributions

Lepik M conceived the review, conducted the literature search, and drafted the manuscript. Chevalier N contributed the molecular docking and ADMET-modelling context and critically revised the manuscript. Byrne E contributed the pharmacological and clinical-translation framing and approved the final version for submission.

Ethics Statement

Not applicable. This is a narrative review of previously published molecular docking and ADMET literature and did not involve new experimental data, human participants, or animal subjects.

Data Availability

No new data were generated or analyzed for this review. All sources synthesized are cited in the reference list and are available through their original publishers.

References

1. Murota K, Nakamura Y, Uehara M. Flavonoid metabolism: the interaction of metabolites and gut microbiota. Biosci Biotechnol Biochem. 2018;82(4):600-610. doi:10.1080/09168451.2018.1444467

2. Lam TP, Tran NVN, Pham LHD, Lai NVT, Dang BTN, Truong NLN, Nguyen-Vo SK, Hoang TL, Mai TT, Tran TD. Flavonoids as dual-target inhibitors against alpha-glucosidase and alpha-amylase: a systematic review of in vitro studies. Nat Prod Bioprospect. 2024;14:1. doi:10.1007/s13659-023-00424-w

3. Ostadmohammadi V, Milajerdi A, Ayati E, Kolahdooz F, Asemi Z. Effects of quercetin supplementation on glycemic control among patients with metabolic syndrome and related disorders: a systematic review and meta-analysis of randomized controlled trials. Phytother Res. 2019;33(5):1330-1340. doi:10.1002/ptr.6334

4. Jhong CH, Riyaphan J, Lin SH, Chia YC, Weng CF. Screening alpha-glucosidase and alpha-amylase inhibitors from natural compounds by molecular docking in silico. BioFactors. 2015;41(4):242-251. doi:10.1002/biof.1219

5. Kim JS, Kwon CS, Son KH. Inhibition of alpha-glucosidase and amylase by luteolin, a flavonoid. Biosci Biotechnol Biochem. 2000;64(11):2458-2461. doi:10.1271/bbb.64.2458

6. Hua F, Zhou P, Wu HY, Chu GX, Xie ZW, Bao GH. Inhibition of alpha-glucosidase and alpha-amylase by flavonoid glycosides from Lu'an GuaPian tea: molecular docking and interaction mechanism. Food Funct. 2018;9(8):4173-4183. doi:10.1039/c8fo00562a

7. Trott O, Olson AJ. AutoDock Vina: improving the speed and accuracy of docking with a new scoring function, efficient optimization, and multithreading. J Comput Chem. 2010;31(2):455-461. doi:10.1002/jcc.21334

8. Daina A, Michielin O, Zoete V. SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. Sci Rep. 2017;7:42717. doi:10.1038/srep42717

9. Pires DEV, Blundell TL, Ascher DB. pkCSM: predicting small-molecule pharmacokinetic and toxicity properties using graph-based signatures. J Med Chem. 2015;58(9):4066-4072. doi:10.1021/acs.jmedchem.5b00104

10. Kahksha, Alam O, Al-Keridis LA, Khan J, Naaz S, Alam A, Ashraf SA, Alshammari N, Adnan M, Beg MA. Evaluation of antidiabetic effect of luteolin in STZ induced diabetic rats: molecular docking, molecular dynamics, in vitro and in vivo studies. J Funct Biomater. 2023;14(3):126. doi:10.3390/jfb14030126

11. Proenca C, Freitas M, Ribeiro D, Tome SM, Oliveira EFT, Viegas MF, Araujo AN, Ramos MJ, Silva AMS, Fernandes PA, Fernandes E. Evaluation of a flavonoids library for inhibition of pancreatic alpha-amylase towards a structure-activity relationship. J Enzyme Inhib Med Chem. 2019;34(1):577-588. doi:10.1080/14756366.2018.1558221

12. Ahmed S, Ali MC, Ruma RA, Mahmud S, Paul GK, Saleh MA, Alshahrani MM, Obaidullah AJ, Biswas SK, Rahman MM, Rahman MM, Islam MA. Molecular docking and dynamics simulation of natural compounds from betel leaves (Piper betle L.) for investigating the potential inhibition of alpha-amylase and alpha-glucosidase of type 2 diabetes. Molecules. 2022;27(14):4526. doi:10.3390/molecules27144526

13. Kaliaperumal K, Zhang L, Gao L, Xiong Q, Liang Y, Jiang Y, Zhang J. Insight into the inhibitory mechanisms of hesperidin on alpha-glucosidase through kinetics, fluorescence quenching, and molecular docking studies. Foods. 2023;12(22):4142. doi:10.3390/foods12224142

14. McMillan J, Bester MJ, Apostolides Z. In silico docking and ADMET studies on clinical targets for type 2 diabetes correlated to in vitro inhibition of pancreatic alpha-amylase and alpha-glucosidase by rutin, caffeic acid, p-coumaric acid, and vanillin. In Silico Pharmacol. 2025;13:42. doi:10.1007/s40203-025-00324-6

15. Pan J, Zhang Q, Zhang C, Yang W, Liu H, Lv Z, Liu J, Jiao Z. Inhibition of dipeptidyl peptidase-4 by flavonoids: structure-activity relationship, kinetics and interaction mechanism. Front Nutr. 2022;9:892426. doi:10.3389/fnut.2022.892426

16. Lalitha N, Sadashivaiah B, Ramaprasad TR, Singh SA.

Anti-hyperglycemic activity of myricetin, through inhibition of DPP-4 and enhanced GLP-1 levels, is attenuated by co-ingestion with lectin-rich protein. PLOS ONE. 2020;15(4):e0231543. doi:10.1371/journal.pone.0231543

17. Meduru H, Wang YT, Tsai JJP, Chen YC. Finding a potential dipeptidyl peptidase-4 (DPP-4) inhibitor for type-2 diabetes treatment based on molecular docking, pharmacophore generation, and molecular dynamics simulation. Int J Mol Sci. 2016;17(6):920. doi:10.3390/ijms17060920

18. Baranowska J, Kiss A, Szeleszczuk Ł. Molecular docking of natural compounds as DPP-4 inhibitors in type 2 diabetes: a comprehensive review. Pharmaceutics. 2026;18(6):741. doi:10.3390/pharmaceutics18060741

19. Salam NK, Huang THW, Kota BP, Kim MS, Li Y, Hibbs DE. Novel PPAR-gamma agonists identified from a natural product library: a virtual screening, induced-fit docking and biological assay study. Chem Biol Drug Des. 2008;71(1):57-70. doi:10.1111/j.1747-0285.2007.00606.x

20. Singh AK, Raj V, Keshari AK, Rai A, Kumar P, Rawat A, Maity B, Kumar D, Prakash A, De A, Samanta A, Bhattacharya B, Saha S. Isolated mangiferin and naringenin exert antidiabetic effect via PPARgamma/GLUT4 dual agonistic action with strong metabolic regulation. Chem Biol Interact. 2018;280:33-44. doi:10.1016/j.cbi.2017.12.007

21. Yoshida H, Tsuhako R, Atsumi T, Narumi K, Watanabe W, Sugita C, Kurokawa M. Naringenin interferes with the anti-diabetic actions of pioglitazone via pharmacodynamic interactions. J Nat Med. 2017;71(2):442-448. doi:10.1007/s11418-016-1063-4

22. Moon DO. Plant-derived flavonoids as AMPK activators: unveiling their potential in type 2 diabetes management through mechanistic insights, docking studies, and pharmacokinetics. Appl Sci. 2024;14(19):8607. doi:10.3390/app14198607

23. Bitew M, Desalegn T, Demissie TB, Belayneh A, Endale M, Eswaramoorthy R. Pharmacokinetics and drug-likeness of antidiabetic flavonoids: molecular docking and DFT study. PLOS ONE. 2021;16(12):e0260853. doi:10.1371/journal.pone.0260853

24. Graefe EU, Wittig J, Mueller S, Riethling AK, Uehleke B, Drewelow B, Pforte H, Jacobasch G, Derendorf H, Veit M. Pharmacokinetics and bioavailability of quercetin glycosides in humans. J Clin Pharmacol. 2001;41(5):492-499. doi:10.1177/00912700122010366

25. Moon YJ, Wang L, DiCenzo R, Morris ME. Quercetin pharmacokinetics in humans. Biopharm Drug Dispos. 2008;29(4):205-217. doi:10.1002/bdd.605

26. Barve A, Chen C, Hebbar V, Desiderio J, Saw CL, Kong AN. Metabolism, oral bioavailability and pharmacokinetics of chemopreventive kaempferol in rats. Biopharm Drug Dispos. 2009;30(7):356-365. doi:10.1002/bdd.677

27. Zeng H, Liu C, Wan L, Peng L, Wen S, Fang W, Chen H, Wang K, Yang X, Huang J, Liu Z. (-)-Epicatechin ameliorates type 2 diabetes mellitus by reshaping the gut microbiota and Gut-Liver axis in GK rats. Food Chem. 2024;447:138916. doi:10.1016/j.foodchem.2024.138916