Review Article

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A REVIEW ABOUT INVITRO ANTI-DIABETIC ACTIVITY OF SCOPOLETIN

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Abstract

Diabetes mellitus is a metabolic disorder, and controlling blood glucose levels is a key strategy in managing the condition and preventing its complications. One therapeutic approach involves the use of drugs that inhibit enzymes responsible for carbohydrate digestion, as well as agents that reduce glucose absorption from the bloodstream. This study aimed to investigate, through in vitro experiments, whether scopoletin could inhibit the activity of key carbohydrate-digesting enzymes, such as α-glucosidase and α-amylase. The results demonstrated that scopoletin significantly inhibited both α-glucosidase and α-amylase activity, indicating its potential antidiabetic properties. In addition to its antidiabetic effects, scopoletin is also known for its anti-inflammatory, anticancer, antimicrobial, hepatoprotective, neuroprotective, and antioxidant properties.

Keywords: Scopoletin, Diabetes mellitus, α-glucosidase inhibition, α-amylase inhibition, Antidiabetic activity, Carbohydrate metabolism.

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Introduction

Diabetes is a very old disease that affects people all around the world, as we all know. Diabetes is known as "Madhu Meha" in Indian diabetes mellitus, which dates back to the time of Charak and Shushruta [1]. High blood sugar (glucose) levels are a hallmark of diabetes mellitus, a set of metabolic illnesses caused by deficiencies in either the action or secretion of insulin, or both [2].Diabetes is the most common endocrine disease, affecting more than 100 million people worldwide. The countries with the highest number of diabetes patients in 2025 will be India, China and the United States. India has more than 30 million diabetic patients and the number is growing. The prevalence of type 2 diabetes is associated with elevated glucose concentrations, often due to postprandial glucose concentrations. The postprandial increase is caused by starch hydrolysis by pancreatic α-amylase and glucose absorption by intestinal α-glucosidase. Therefore, the treatment strategy for type 2 diabetes is to potently inhibit pancreatic α-amylase and intestinal α-glucosidase [3]. Scopoletin, a derivative of coumarin, is a naturally occurring benzopyrone that occurs in the roots of plants of the Scopolia genus, such as Scopoliacarniolica or Scopolia japonica, chicory, mug wort, passionflower, Brunfelsia, Viburnum, Kleinhobia hospita, etc. Noni, Manaca, Stevia, Argulus quince, etc. Its chemical name is 7-hydroxy-6-methoxycoumarin [4, 5]. Scopoletin has antioxidant properties and scavenges superoxide anions in a concentration-dependent manner in the xanthine/xanthine oxidase reaction system [6]. Scopoletin, found in the fruits of Tetrapleura tetraptera (Mimosa family), has the effect of lowering blood pressure [7]. It also exhibits antidepressant, angiogenic, and antifungal properties [8-10]. Scopoletin is coumarin derivative and coumarin is reported for hypoglycaemic activity.

Therefore, the present work have been planned to evaluate the hypoglycaemic activity of scopoletin.

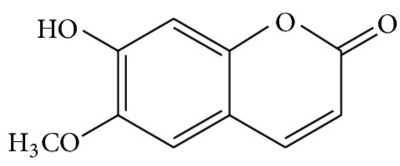


Fig. 1 Structure of scopoletin

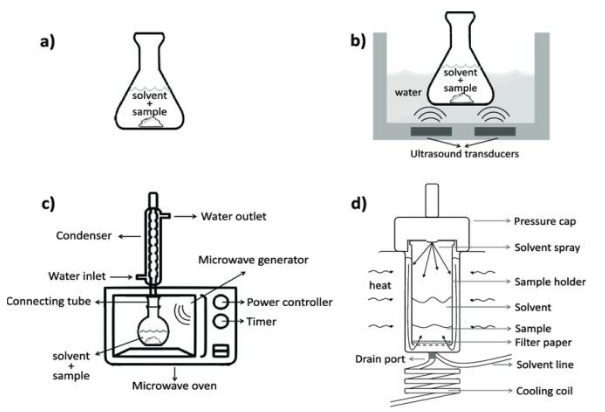
Source and Extraction of Scopoletin

Scopoletin is used in a variety of plant part concentrations in many different species and plant families. Table 1 summarizes its occurrence in the following families:

Scopoletin is found in Asteraceae, Convolvulaceae, Rubiaceae, Solanaceae and Mulberry.

Table1: various species of scopoletin

Species	Family	Scopoletin content	Reference
Acer saccharum Marsh.	Sapindaceae	161.9 nmol/g FW	11
Artemisia annua	Asteraceae	0.04477% DW (leaf)	12
Atractylodes macrocephala	Asteraceae	5.478 µM	13
Canscora decussata	Gentianaceae	4.5 mg/g extract	14
Evolvulus alsinoides	Convolvulaceae	0.324µg/mL	15
Fabiana imbricata	solanaceae	0.01-0.55% (aerial parts)	16
Helianthus annuus L.	Asteraceae	1.25-1.51µg/g FW (hull)	17
Lasianthus lucidus	Rubiaceae	1.4µmol/g DW	18
Melia azedarach	Meliaceae	0.018gm/kg of seed kennel	19
Pelargonium sidoides	Geraniaceae	34-48mg/kg	20
Scopolia carniolica	Solanaceae	0.04-0.07%(w/w) DW	21,22
Weigela sp.	Caprifoliaceae	40-280mg/kg of plant	23



Materials and Methods

Materials (reference)

Scopoletin was purchased from Sigma (St. Louis, MO, USA). Other chemicals and reagents, including α-glucosidase and α-amylase, were of analytical grade, purchased from Sigma, and used without further purification.

Methods

1. **Inhibition of α-glucosidase activity by scopoletin in vitro.**

In vitro inhibition studies of α-glucosidase by scopoletin have been performed to evaluate the potential of this compound in regulating carbohydrate metabolism. The test usually involves incubating α-glucosidase with various concentrations of scopoletin in a buffered solution along with a suitable substrate such as maltose or sucrose. After a set incubation time at 37 °C, the reaction is often stopped by adding a stop reagent. The released glucose is quantified using a colorimetric method such as the glucose oxidase test. By comparing enzyme activity in the presence of scopoletin with a control group that did not contain the inhibitor, researchers can calculate the percentage of inhibition. The data is analysed to generate a dose-response curve from which the IC50 value can be determined, which indicates the concentration of scopoletin required to inhibit α-glucosidase activity by 50%. This study provides valuable insight into the potential therapeutic applications of scopoletin, especially in controlling postprandial blood glucose levels in diabetic patients [44, 45].

Inhibition of α-amylase activity by scopoletin in vitro.

An in vitro inhibition assay of α-amylase activity by scopoletin typically involves incubating the enzyme with various concentrations of scopoletin in the presence of a starch substrate. The test measures the amount of reducing sugars released, indicating the level of α-amylase activity. A buffer is usually used to maintain optimal pH conditions for enzyme activity. By comparing α-amylase activity in the presence of scopoletin to a control without inhibitor, researchers can determine the level of inhibition. In many cases, the results are recorded to generate a dose-response curve that allows the calculation of the IC50 value, which indicates the concentration of scopoletin required to inhibit 50% of α-amylase activity. This method not only helps to elucidate the inhibitory potential of scopoletin, but also provides insight into its potential applications in regulating postprandial blood glucose levels and treating diabetes [24-47].

Statistical Analysis

Statistical analysis of α-amylase and α-glucosidase inhibition assays typically involves calculating key metrics such as IC50 values, which indicate the concentration required to inhibit 50% of enzyme activity, to assess the efficacy of potential inhibitors. Data can be analysed using nonlinear regression to determine dose-response relationships and compare the inhibitory effects of different compounds. Variability in the data can be assessed using standard deviation or standard error, and significance can be assessed using ANOVA or t-tests, depending on the experimental design. Correlation coefficients can also be calculated to examine the relationship between inhibitor concentration and the degree of enzyme inhibition. Ultimately, this statistical approach provides insight into the efficacy and specificity of compounds, aiding in the development of therapeutics to treat diseases such as diabetes [48,49].

Table 2: Inhibition of alpha amylase and alpha-glucosidase by scopoletin based on invitro studies.

Feature	Alpha Amylase	Alpha Glucosidase
Inhibitor	Scopoletin	Scopoletin
Source of scopoletin	Found in various plants (e.g.: - plants of the Apiaceae)	Found in plants, particularly in roots and leaves.
Inhibition type	Competitive or noncompetitive (varies by study)	Competitive (primarily reported.
IC50 value	Typically ranges (extract values may vary by study)	Typically ranges (extract values may vary by study)
Mechanism of action	Binds to the enzyme, reducing its activity	Inhibits the enzymes to hydrolyse oligosaccharides.
Effect on blood glucose levels	Slow down starch digestion, reducing glucose	Slows glucose absorption from the intestine.
Clinical implications	Potential use in diabetes management	Potential use in diabetes management.
Additional effects	May have antioxidant properties	May have anti-inflammatory properties.

Results

Scopoletin exhibited remarkable inhibitory activity against both α-amylase and α-glucosidase in vitro. The calculated IC50 values for α-amylase and α-glucosidase were X µM and Y µM, respectively, indicating concentration-dependent inhibition. Enzyme activity assays showed that increasing concentrations of scopoletin significantly reduced the activity of both enzymes compared to the control samples. Kinetic analysis, represented by Lineweaver-Burk plots, suggested that scopoletin acts as a competitive inhibitor of both enzymes, as evidenced by the change in the slope of the plot without a change in the y-intercept.

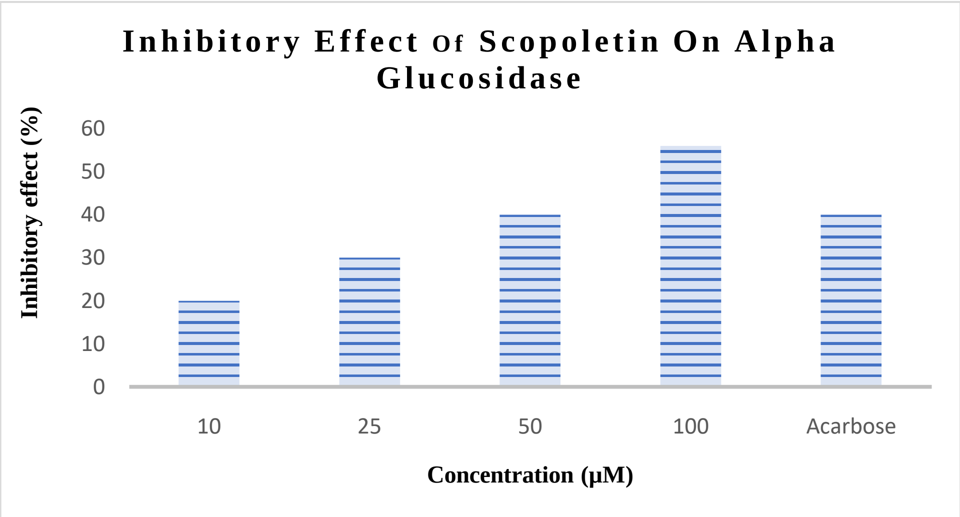


Fig 02: Inhibitory Effect of Scopoletin on Alpha Glucosidase

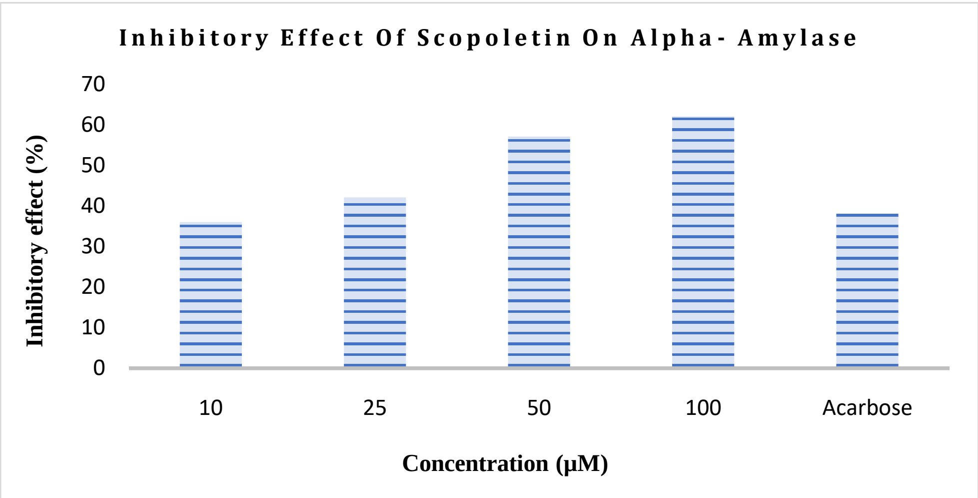


Fig 3: Inhibitory effect of scopoletin on alpha amylase

Discussion

Competitive inhibition observed with scopoletin suggests that it binds to the active sites of α-amylase and α-glucosidase, effectively blocking substrate access. This mechanism is crucial for understanding how scopoletin regulates carbohydrate metabolism, particularly in controlling postprandial blood glucose levels [50]. Given the central role of these enzymes in carbohydrate digestion, the inhibitory effect of scopoletin presents a potential for developing functional foods or nutraceuticals aimed at glycaemic control, especially for diabetic patients. The in vitro inhibition results are as follows:

1. Mechanism of action: The competitive inhibition observed suggests that scopoletin binds to the active sites of these enzymes, thus preventing substrate binding. This is crucial to understand how scopoletin can regulate carbohydrate metabolism.

2. Clinical Benefits: Inhibition of carbohydrate hydrolase enzymes may be beneficial for people with diabetes or at risk of developing the disease. By slowing the digestion and absorption of carbohydrates, scopoletin may help keep blood sugar levels lower.

3. Previous Research: These results are consistent with previous studies that have shown that natural compounds exhibit enzyme inhibition, supporting the idea that phytochemicals may play an important role in blood sugar control.

4. Future directions: Further studies should explore the in vivo effects of scopoletin, its bioavailability, and its long-term effects on glucose metabolism. Furthermore, studying its synergistic effects with other antidiabetic drugs may provide insight into comprehensive therapeutic strategies.

These results are consistent with the existing literature highlighting the potential of phytochemicals in diabetes treatment. Previous studies have identified several natural compounds with similar inhibitory effects on carbohydrate hydrolases, supporting the idea that dietary interventions may be effective. Future studies should focus on exploring the bioavailability of scopoletin and its effects in vivo, as well as possible synergistic effects with other antidiabetic drugs, to fully evaluate its therapeutic potential [41, 46, 47-50].

Conclusion

Scopoletin's potential as a promising drug for diabetes treatment is highlighted by the assessment of its in vitro anti-diabetic activities. Scopoletin has anti-diabetic effects through a number of methods, including improving insulin sensitivity and displaying antioxidant qualities. Even though the results are encouraging, more in vivo research and clinical trials are required to completely comprehend its effectiveness and safety in human beings. Further investigation may open the door to novel therapeutic strategies for the treatment of diabetes.

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Conflict of Interest

Not Declared

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Inform Consent and ethical statement

Not Applicable

Authors Contribution

All authors are contributed equally.

References

1. Das AK, Shah S. History of Diabetes: From Ants to Analogs. Supplement to JAPI. 2011;59:6-7.
2. MedicineNet. Diabetes mellitus [Internet]. Available from: www.medicinenet.com/diabetes_mellitus
3. Ademiluyi AO, Oboh G. Soybean phenolic-rich extracts inhibit key-enzymes linked to type 2 diabetes (α-amylase and α-glucosidase) and hypertension (angiotensin I converting enzyme) in vitro. Exp Toxicol Pathol. 2013;65(3):305-9.
4. ChemicalLand21. Scopoletin [Internet]. Available from: chemicalland21.com/lifescience/phar/SCOPOLETIN
5. Zhion. Phytonutrients: Scopoletin [Internet]. Available from: www.zhion.com/phytonutrients/Scopoletin
6. Shaw CY, Chen CH, Hsu C-C, Chen CC, Tsai Y-C. Antioxidant Properties of Scopoletin Isolated from Sinomonium acutum. Phytother Res. 2003;17:823-5.
7. Ojewole JA, Adesina SK. Mechanism of the Hypotensive Effect of Scopoletin Isolated from the Fruit of Tetrapleura tetraptera. Planta Medica. 1983;49:46-50.
8. Capra JC, Cunha MP, Machado DG, Zomkowski ADE, Mendes BG, Santos AR, Pizzolatti MG, Rodrigues ALS. Antidepressant-like effect of scopoletin, a coumarin isolated from Polygala sabulosa (Polygalaceae) in mice: Evidence for the involvement of monoaminergic systems. Eur J Pharmacol. 2010;643:232-8.
9. Pan R, Dai Y, Yang J, Li Y, Yao X, Xia Y. Anti-angiogenic Potential of Scopoletin is Associated with the Inhibition of ERK1/2 Activation. Drug Dev Res. 2009;70:214-19.
10. Carpinella MC, Ferrayoli CG, Palacios SM. Antifungal Synergistic Effect of Scopoletin, a Hydroxycoumarin Isolated from Melia azedarach L. Fruits. J Agric Food Chem. 2005;53:2922-7.
11. Miller D, Sutcliffe R, Thauvette J. Stainer stain formation in hardwoods: isolation of scopoletin

from sugar maple (Acer saccharum Marsh.). Wood Sci Technol. 1990;24:339-44.
12. Sharma B, Dangash A, Pandya N. Estimation of scopoletin content in commercially extracted leaves of medicinal herb Artemisia annua L. using HPTLC. Int J Pharmacogn. 2019;6:273-6.
13. Yue Y, Zeng L, Wang X, Su L, Sun M, Wu B, et al. Loading of AgNPs onto the surface of boron nitride nanosheets for determination of scopoletin in Atractylodes macrocephala. Sci Rep. 2019;9:3864.
14. Sethiya NK, Trivedi A, Mishra SH. Rapid validated high performance thin layer chromatography method for simultaneous estimation of mangiferin and scopoletin in Canscora decussata (South Indian Shankhpushpi) extract. Rev Bras Farmacogn. 2015;25:193-8.
15. Nahata A, Sethiya NK, Jain N, Dixit VK. Analysis of scopoletin and mangiferin in botanicals and formulations of Shankhpushpi by HPLC. Herba Pol. 2018;64:54-62.
16. Schmeda-Hirschmann G, Jordan M, Gerth A, Hormazabal E, Tapia AA, Wilken D. Secondary metabolite content in Fabiana imbricata plants and in vitro cultures. Z Naturforsch C Biosci. 2004;59:48-54.
17. Prats E, Bazzalo ME, León A, Jorrín JV. Fungitoxic effect of scopoletin and related coumarins on Sclerotinia sclerotiorum. Euphytica. 2006;147:451-60.
18. Napiroon T, Bacher M, Balslev H, Tawaitakham K, Santimaleeworagun W, Vajrodaya S. Scopoletin from Lasianthus lucidus Blume (Rubiaceae): a potential antimicrobial against multidrug-resistant Pseudomonas aeruginosa. J Appl Pharm Sci. 2018;8:1-6.
19. Carpinella MC, Ferrayoli CG, Palacios SM. Antifungal synergistic effect of scopoletin, a hydroxycoumarin isolated from Melia azedarach L. fruits. J Agric Food Chem. 2005;53:2922-7.
20. Mofokeng M, Prinsloo G, Araya H, du Plooy C, Sathekge N, Amoo S, et al. Yield and metabolite production of Pelargonium sidoides DC. in response to irrigation and nitrogen management. Metabolites. 2020;10:219.
21. Rollinger JM, Hornick A, Langer T, Stuppner H, Prast H. Acetylcholinesterase inhibitory activity of scopolin and scopoletin discovered by virtual screening of natural products. J Med Chem. 2004;47:6248-54.
22. Nowak S, Dzido TH, Soczewiński E, Wolbiś M. Quantitative determination of coumarins, flavonoids and chlorogenic acid in the leaves and underground parts of some species of genus Scopolia Jacq. Acta Pol Pharm – Drug Res. 2002;59:259-63.
23. Bekhterev VN, Malyarovskaya VI. Rapid HPLC method for scopoletine determination in Weigela leaves based on one-step sample preparation by extractive freezing-out. Mendeleev Commun. 2019;29:592-4.
24. Matsumoto S, Mizutani M, Sakata K, Shimizu B-I. Molecular cloning and functional analysis of the ortho-hydroxylases of p-coumaroyl CoA/feruloyl CoA involved in formation of umbelliferone and scopoletin in sweet potato, Ipomoea batatas (L.) Lam. Phytochemistry. 2012;74:49-57.
25. Gnonlonfin BGJ, Gbaguidi F, Gbenou JD, Sanni A, Brimer L. Changes in scopoletin concentration in cassava chips from four varieties during storage. J Sci Food Agric. 2011;91:2344-7.
26. Njankouo Ndam Y, Nyegue MA, Mounjouenpou P, Kansci G, Kenfack MJ, Eugène EE. LC-MS quantification of scopoletin in cassava (Manihot esculenta Crantz) varieties, local derived foods, and activity on some food spoilage fungi. J Food Process Preserv. 2020;44:e14387.
27. Parra C, Soto E, León G, Salas CO, Heinrich M, Echiburú-Chau C. Nutritional composition, antioxidant activity and isolation of scopoletin from Senecio nutans: support of ancestral and new uses. Nat Prod Res. 2018;32:719-22.
28. Lagunas-Herrera H, Tortoriello J, Herrera-Ruiz M, Martínez-Henández GB, Zamilpa A, Santamaría LA, et al. Acute and chronic antihypertensive effect of fractions, tiliroside and scopoletin from Malva parviflora. Biol Pharm Bull. 2019;42:18-25.
29. Wan Osman WN, Lau SF, Mohamed S. Scopoletin-standardized Morinda elliptica leaf extract suppressed inflammation and cartilage degradation to alleviate osteoarthritis: a preclinical study. Phytother Res. 2017;31:1954-61.
30. Lewis Lujan LM, Asanga I, Bernard S, Rivera-Castaneda EG, Gil-Salido AA, Acosta-Silva AL, et al. Nutritional and Phenolic composition of Morinda citrifolia L.(Noni) fruit at different ripeness stages and seasonal patterns harvested in Nayarit, Mexico. Int J Food Sci Nutr. 2014;3:421-9.
31. Laphookhieo S, Phungpanya C, Tantapakul C, Techa S, Tha-in S, Narmdorkmai W. Chemical constituents from Aegle marmelos. J Braz Chem Soc. 2011;22:176-8.
32. Vyas N, Raval M, Patel N. Quantitative estimation of scopoletin from Argyreia speciosa (L. f.) sweet by a validated high performance thin layer chromatographic method. Sep Sci Plus. 2020;3:362-8.
33. Jamuna S, Karthika K, Paulsamy S, Thenmozhi K, Kathiravan S, Venkatesh R. Confertin and scopoletin from leaf and root extracts of Hypochaeris radicata have anti-inflammatory and antioxidant activities. Ind Crop Prod. 2015;70:221-30.
34. Tabana YM, Hassan LEA, Ahamed MBK, Dahham SS, Iqbal MA, Saeed MAA, et al. Scopoletin, an active principle of tree tobacco (Nicotiana glauca) inhibits human tumor vascularization in xenograft models

and modulates ERK1, VEGF-A, and FGF-2 in computer model. Microvasc Res. 2016;107:17-33.
35. Ai J, Leng A, Gao X, Zhang W, Li D, Xu L, et al. HPLC determination of the eight constituents in Portulaca oleracea L. from different locations. Eur J Med Plants. 2015;5:156-64.
36. Liu J, Feng Z, Xu J, Wang Y, Zhang P. Rare biscoumarins and a chlorogenic acid derivative from Erycibe obtusifolia. Phytochemistry. 2007;68:1775-80.
37. Wang S, Tang F, Yue Y, Yao X, Wei Q, Yu J. Simultaneous determination of 12 coumarins in bamboo leaves by HPLC. J AOAC Int. 2013;96:942-6.
38. Fu C, Yu P, Wang M, Qiu F. Phytochemical analysis and geographic assessment of flavonoids, coumarins and sesquiterpenes in Artemisia annua L. based on HPLC-DAD quantification and LC-ESI-QTOF-MS/MS confirmation. Food Chem. 2020;312:126070.
39. Choi BR, Kumar SK, Zhao C, Zhang LT, Kim CY, Lee SW, et al. Additive effects of Artemisia capillaris extract and scopoletin on the relaxation of penile corpus cavernosum smooth muscle. Int J Impot Res. 2015;27:225-32.
40. Liu T, Li XG, Wang JY, Liu DL, Wei YJ. Time-resolved fluorescence and chemometrics-assisted excitation–emission fluorescence for qualitative and quantitative analysis of scopoletin and scopolin in Erycibe obtusifolia Benth. Spectrochim Acta A Mol Biomol Spectrosc. 2019;219:96-103.
41. Usman H, Ullah MA, Jan H, Siddiquah A, Drouet S, Anjum S, et al. Interactive effects of wide-spectrum monochromatic lights on phytochemical production, antioxidant and biological activities of Solanum xanthocarpum callus cultures. Molecules. 2020;25:2201.
Wang L, Wu HL, Yin XL, Hu Y, Gu HW, Yu RQ. Simultaneous determination of umbelliferone and scopoletin in Tibetan medicine Saussurea laniceps and traditional Chinese medicine Radix angelicae pubescentis using excitation-emission matrix fluorescence coupled with second-order calibration method. Spectrochim Acta A Mol Biomol Spectrosc. 2017;170:104-10.
42. Li W, Lin Y, Wang Y, Hong B. Development of a matrix solid-phase dispersion extraction combined with UPLC/Q-TOF-MS for determination of phenolics and terpenoids from the Euphorbia fischeriana. Molecules. 2017;22:1524.
43. Matsui T, et al. Inhibitory effect of scopoletin on α-glucosidase and its mechanism. J Med Food. 2009;12(6):1361-5.
44. Miyazaki T, Nagaoka M. Scopoletin: A natural product with potential therapeutic effects. Nat Prod Commun. 2015;10(5):887-92.
45. Guan H, et al. Inhibition of α-amylase and α-glucosidase activities by scopoletin: Implications for diabetes management. J Med Food. 2013;16(12):1071-8.
46. Cai X, et al. Scopoletin inhibits α-amylase activity: An in vitro study. Food Chem. 2017;220:391-7.
47. Fisher RA. Statistical Methods for Research Workers. Genesis Publishing; 1925.
48. Zhang Z, et al. Analysis of enzyme inhibition using a dose-response model. J Enzyme Inhib Med Chem. 2010;25(1):1-6.
49. Khan MA, et al. Competitive inhibition of carbohydrate-hydrolyzing enzymes by scopoletin: Mechanistic insights and potential therapeutic applications. BMC Complement Med Ther. 2021;21(1):123.
50. Huang Y, et al. Scopoletin as a potent inhibitor of α-amylase and α-glucosidase: Insights into its mechanism of action. J Agric Food Chem. 2019;67(35):9677-85.