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REVIEW ON NARINGIN: METHOD OF ISOLATION, ANALYTICAL DEVELOPMENT, AND ITS RECENT PHARMACOLOGICAL ACTIVITIES

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ABSTRACT: Naringin is a flavonoid isolated from different citrus fruits like Grapefruit, Orange, Pomelo, Lemon, *etc*, which are commonly called local fruit. Naringin is found in the white spongy portion of citrus peel. Its content varies from 0.65 mg/gm in the mandarin peel to 14.40mg/gm in the grapefruit peel. Naringin is metabolized to the flavanone naringenin by the enzyme Naringinase present in the liver. It can be analyzed by using various analytical techniques such as HPLC, TLC, UV, HPTLC, mass spectroscopy, Liquid chromatography, chiral chromatography and LC/Mass spectroscopy. Naringin can act as an antioxidant and scavenge free radicals. Naringin mainly focuses on *in-vitro* and *in-vivo* animal studies showing its beneficial effects on cardioprotective, antioxidant, anti-inflammatory, antimicrobial, hypolipemiant, neurological, thermogenic, pulmonary disorders and antidiabetic. Naringin is also treated as a most promising treatment strategy against Covid-19 due to its antiviral and anti-inflammatory effects. Recently, Naringin has proven its activity in various molecular docking studies. Naringin keeps the body healthy against various illnesses and major lifestyle disorders.

INTRODUCTION: Nowadays, scientists are more interested in naturally occurring drugs. Naturally obtained drugs are rich in their secondary metabolites, becoming popular in treating different diseases, and have also proven success stories among patients. Also, herbs are economical, easily available, reduce adverse drug reactions, and reduce rehospitalization. These insights made herbs proven to be possible as a promising agent for future perspective. Numerous studies have been included in the pharmaceutical sciences, such as anti-diabetic, hepatoprotective, free radical scavenging activity, and anti-hyperlipidemic [1, 2, 3]. Citrus fruits are a good source of flavonoids.

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Naringin (NAR) is a common flavonoid in citrus fruits like Grapefruit, Orange, Pomelo, Lemon, *etc*. All these fruits are easily available in India, called local fruit or seasonal fruit. The proportion of Naringin is found in each citrus depends on the variety of fruit, state of ripening, and the climatic conditions it has been exposed to. Citrus fruits are a good source of antioxidants, especially flavonoids, which are mainly two types; flavanone glycoside and polymethoxylated glycoside [4-6].

It contains a mainly bitter principle isolated in 1866 by De Vry in Java from grapefruit blossoms. It exerts various pharmacological effects such as antioxidant, blood lipid-lowering, anticarcinogenic activity & anti-diabetic activity. It also inhibits the selected cytochrome P450 enzymes, including CYP3A4 & CYP1A2, which may result in several drug interactions *in-vitro*. In human Naringin is metabolised to the flavanone Naringenin. Naringin is also a most promising treatment strategy against Covid-19 due to its antiviral and anti-inflammatory

effects. It is proven that the consumption of either grapefruit, orange, or Naringin itself keeps the body healthy and active against various illnesses. It is highly active against various major lifestyle disorders and even as an antineoplastic agent [7]. The class of flavanones is specific to citrus products (fruit, juice). They largely contribute to the total daily flavonoid intake range is 150-600 mg/day. Among flavanones found in Citrus co-products, Naringin has interesting biologic activities like antioxidant and antimutagenic activities. Naringin can reduce the level of cholesterol in the plasma, reduce the risk of atherosclerosis, protect the level of vitamin E in the plasma, enhance flavors for sweets, drinks and bakery products and stabilize oils. Naringin is found in the white spongy portion of citrus peel. Its content varies from 0.65mg/gm in the mandarin peel to 14.40mg/gm in grapefruit peel [8, 9]. Citrus is the most important cultivated fruit in the world with reported production of about 89 million tons in 2014(USDA, 2014). Estimated 26% of Citrus fruits are industrially processed into juice. The amount of industrial Citrus coproducts is estimated at 15 $\times 10^6$ tons and it consists essentially of seeds, peels, and pulp residue. Indeed, Citrus co-products are rich in bioactive molecules (pigments, fibers, essential oils, flavonoids) which can constitute a high added value for industrialists [10, 11].

Metabolism of Naringin in the Body: In humans, Naringinase is available in the liver, and it rapidly metabolizes naringin into Naringenin. It occurred in two steps- first, Naringin is hydrolyzed by the α-L-rhamnosidase activity of naringinase to rhamnose and prunin. The prunin formed is then hydrolyzed by the β-d-glucosidase activity of Naringinase into Naringenin and glucose. Naringinase is an enzyme that has a wide occurrence in nature; in plants, yeasts, and fungi. It is commercially attractive due to its bitterness removal properties [4-7].

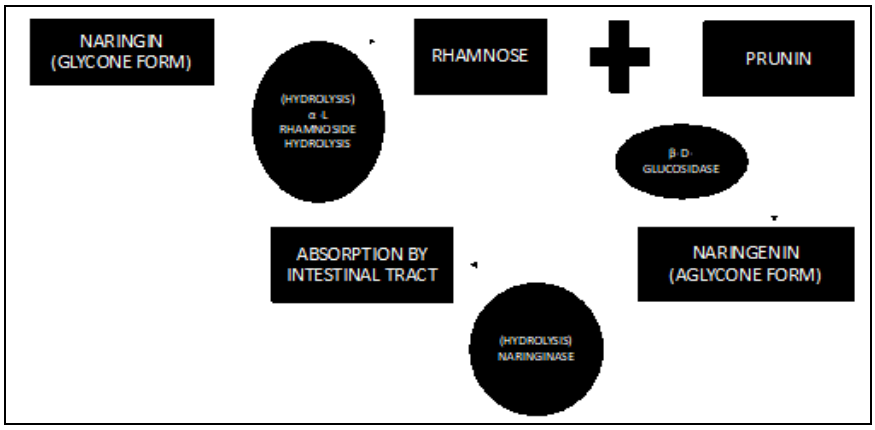

FIG. 1: METABOLISM OF NARINGIN IN THE BODY

Chemistry of Naringin: Flavonoids are composed of two aromatic rings linked to three carbon atoms forming an oxygenated heterocycle. Flavonoids are a widely distributed group of polyphenolic compounds characterized by a common benzo-pyrone structure. Over 4,000 different flavonoids have been described and categorized into flavonols, flavones, flavanones, isoflavones, catechins and anthocyanidins.

Diverse biochemical properties of flavonoids including naringin, hesperidin, diosmin, and rutin have provoked interest in biology and medicinal chemistry. Naringin is a flavanone-7-O-glycoside between the flavanone Naringenin and the Disaccharide neohesperidose. Naringin, the bitter principle of grapefruit (Citrus paradisi), is found in the fruit's juice, flower, and rind and constitutes up to 10% of the dry weight. Naringin and other Naringenin glycosides can be found in a variety of other sources. The flavonoid Naringin occurs naturally in citrus fruit, especially in grapefruit, where Naringin is responsible for the fruit's bitter taste. The chemical formula for Naringin is $C_{27}H_{32}O_{14}$ and its molecular weight is 580.4g/mol. The taste of NAR is bitter, and the color is beige. Its melting point ranges from 165^0C to 170°C. Naringin is highly soluble in organic solvents; Ethanol, Methanol, and Dimethyl Sulfoxide and sparingly soluble in an aqueous buffer. It is stable for up to 2 years if stored at 20°C [43].

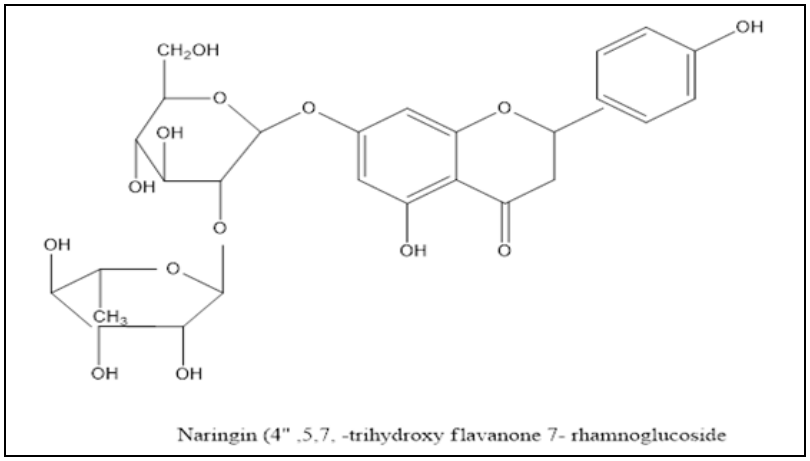

FIG. 2: STRUCTURE OF NARINGIN

Isolation and Extraction of Naringin from Various sources: Isolation is a process by which we can obtain a purified compound, and an extraction process where moving one or more analytes from the sample to a physically separate location where further processing and analysis occurs. Mainly in extraction, it separates the compound from the mixture, and in the isolation process, purification of a compound occurs [9].

TABLE 1: NARINGIN EXTRACTION

Sl. no.	Method Of Extraction	Chemicals	Reference
1	Maceration, Reflux, Supercritical fluid extraction	Ethanol (AR), Carbon dioxide, Nitrogen gas	10
2	Dry albedo/room temperature methanolic extraction (60-70^{0}C for 30 min)	Methanol, Dichloromethane	11
3	Dry albedo/hot methanolic extraction (55 °C for 3 hours)	Methanol, Dichloromethane	11
4	Wet albedo/hot methanolic extraction (55 °C for 3 hours)	Methanol, Dichloromethane	11
5	Liquid phase extraction	Isopropanol, Methanol, n-Hexane	12

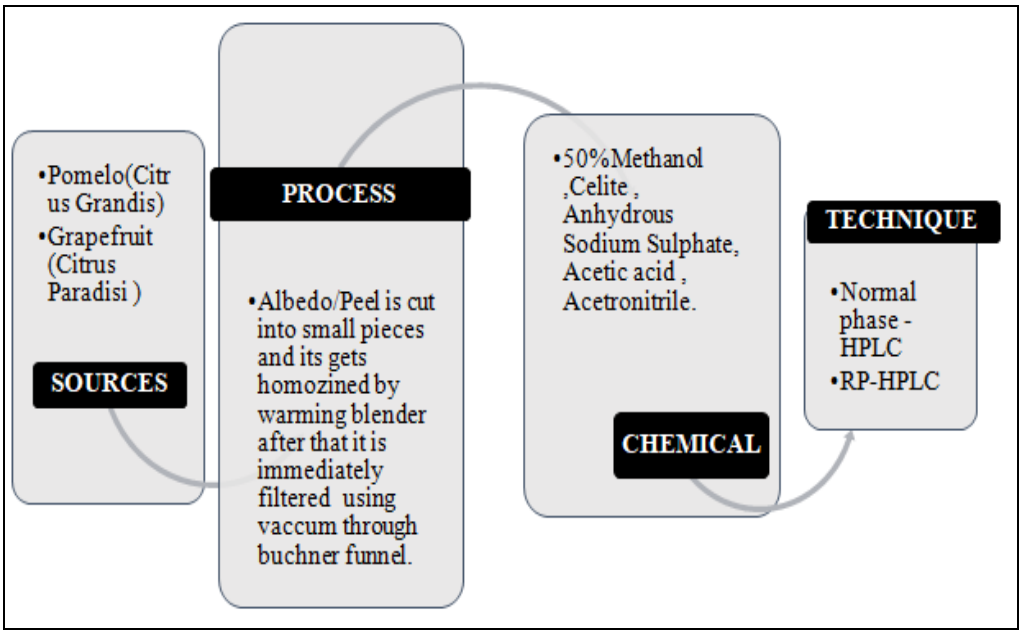

FIG. 3: ISOLATION OF NARINGIN FROM DIFFERENT SOURCES

During the extraction analysis effect of the temperature, light, and oxygen shows that Naringin is a molecule that is very sensitive to its environment. Its degradation begins when

temperatures are superior to 100°Cor in the presence of light. The antioxidant activity of the Naringin solutions varies during their degradation, so the biological activities of the Naringin can be modified during its extraction. In the extraction methods, there are different solvents used. The use of accelerators for solvent extraction is interesting because it makes the procedure less time-consuming. While Naringin, is a polar flavonoid because of that extraction temperature or pressure must be increased to obtain a high Naringin content. So, this temperature or pressure increase can cause Naringin superior to 100°C. During the Naringin extraction, two reactions occurparallelly with increasing extraction temperature or pressure. These two reactions are: (a) an increase of the Naringin released and (b) degradation of Naringin. The study of the effects is monitored; temperature, light and oxygen, showed that Naringin does not degrade with an oxygen content of 85% and for temperatures lower than 100°C. For the preservation of Naringin, direct light needs to avoid. If the extraction temperature is 80°C, it increases the Naringin content since naringin is not affected by temperatures under 100°C. When a temperature above 100°C is applied (microwave power of 400 W), then a decrease in the Naringin content is observed due to a degradation of the Naringin [13].

Analytical Methods for Naringin: Naringin is available as a powder and capsule. Analytical methods were developed for determining Naringin using RP-HPLC, Liquid Chromatography, Mass, HPTLC, LC-mass, and Spectrophotometry.

TABLE 2: REVIEW OF ANALYTICAL METHODS FOR THE ASSAY OF NARINGIN

Sl. no.	Method	Mobile phase (v/v) / Reagent	Column	Reference
1	High-pressure Liquid Chromatographic (HPLC)	The mobile phase consisted of acetonitrile /water Water: Acetronitrile (80:20)	C18 reversed-phase column	10
2	Improved High-pressure Liquid Chromatographic (HPLC)	Mobilephase consisting of methanol and water (38: 62, v/v, pH 3) at a flow rate of 1 ml/min	C18 reversed-phase column (4.6 mm x 250 mm; 10 µm)	15,16
3	RP-HPLC	The mobile phase consisted of tetrahydrofuran / water/acetic acid (21:77:2, v/v/v) and was filtered through a 0.45-mm pore size nylon filter (Alltech, Deerfield, IL, USA) and degassed by ultrasonic treatment before use	Macherey Nagel Nucleosil C8 analytical column (250×4.6 mm, 5µm particle size)	17
4	HPLC	0.05% Formicaqueous solution and 20% Acetonitrile)	C18 column (3.9 mm × 150 mm, 5µm	18
5	HPLC	The mobile phase is acetonitrile/0.1 M ammonium acetate/glacial acetic acid (18:81:0.5, v/v)	Inertsil ODS-2 (Particle size 5 µm) column (250 × 4.6 mm)	19
6	HPLC	Formic acid: Methanol	C18 reverse phase Luna column 4.6 X250 mm	20
7	LC/ESI-MS	The mobile phase was methanol/10 mM ammonium acetate (60:40, v/v)	Nova-Pak C18 column (150 × 3.9 mm	19
8	Tandem mass spectrometry (LC/MS/MS	The mobile phase consisted of methanol (70%) and water (30%)	Beta basic C18 ODS column (100 mm × 2.0 mm 5 µm)	21
9	Liquid Chromatographic	The mobile phase consisted of water-acetonitrile-glacial acetic acid (79.5 + 20 + 0.5, v/v)	RP-C18 column (4.6 mm. x 50mm)	22
10	LC–MS/MS	Acetonitrile and water	Nova Pak C18 column	23
11	Liquid Chromatographic Method	Mobile phase consisted of acetonitrile and potassium phosphate buffer (25.0 mM; pH 3.5 ± 0.1	GraceSmart RP C18 (250.0 × 4.6 mm, 5 μm) column	24
12	Liquid chromatography	The mobile phase consisted of 0.1%	Zorbax SB-C18 analytical	25

	tandem mass spectrometry (LC–MS/MS) method	formic acid water and acetonitrile	column (2.1 mm × 150 mm, 5 µm) (XDB-C18 column (50 x2.1 mm, 1.8 mm)	
13	Colorimetric Method	30/5/60 methanol/acetic acid/water.	μBondapak C, column eluted at a flow rate of 1 ml/min	26
14	Simultaneous Quantification by HPLC	Mobile phase composed of ultra-pure water and acetonitrile	Symmetry C18 reversed-phase column (5-µm particle size, 3×250 mm) and Sep-Pak C18 Plus Short Cartridges	27
15	HPTLC	Ethyl acetate (EA) – EA: Methanol (MeOH)(60:40 v/v)	-	28
16	Chiral high-performance liquid chromatography	n-hexane/ethanol with 0.5% TFA as mobile phase	Chiralpak IB column, (250 mm × 4.6 mm	29
17	HPLC	water-acetonitrile (80:20, v/v)	A Waters Associates 30 cm X 4 mm i.d. reverse phase µBondapak C-18 column	30

TABLE 3: LIST OF ACTIVITIES REPORTED FOR PEEL OF NARINGIN OVER THE LAST 10 YEARS

Sl. no.	Pharmacological Activity	Reference
1	CYP3A4 inhibitor	7(2000)
2	Antidiabetic Effect	31 (2012)
3	Metal chelating effect, anti-microbial, anti-viral, anti-allergic, anti-estrogenic, ischemic heart disease, anti-obesity, Hypoxia	6(2013)
4	Neurodegenerative disorders, osteoporosis, and rheumatological disorders.	5(2014)
5	Obesity, Hypertension, and Metabolic syndrome	8(2014)
6	Anti- -cancer activities, as well as effects on bone regeneration, metabolic syndrome, oxidative stress, genetic damage and central nervous system (CNS) diseases.	32 (2016)
7	Anti-Hyperglycemic, Anti-Hyperlipidemic, Anti-Oxidant	4(2017)
8	Hyperlipidemia, Hypertension, Anti-oxidant, antineoplastic agent, DNA repair, Hepatitis C, Wound healing, Obesity, Anti-Sindbisactivity, Alcohol effect, Antiulcer, Anti-atherogenic, Bioenhancer, Gastroprotective, Bone marrow protective.	33 (2019)
9	Neurogenerative illness	34 (2019)
10	Hepatoprotective,Nephroprotective, Immunomodulatory and Antidiabetic	35 (2019)
11	Cardiovascular diseases, Type 2 Diabetes Mellitus (T2DM), metabolic syndrome, pulmonary disorders,and gastrointestinal pathologies	36 (2021)

TABLE 4: RECENT ACTIVITY OF NARINGIN

Sl. no.	Activity	Result	Reference (Year)
1	Evaluation of the interaction between naringenin and human serum albumin: Insights from fluorescence spectroscopy, electrochemical measurement, and molecular docking	The quenching mechanism of naringin with human serum albumin has been static quenching, the reaction is spontaneous and electrostatic interactions altogether with the hydrogen bonds are the main forces. Nar binding to HSA was confirmed at both site I (subdomain-II A) and site II (subdomain-IIIA), besides the effects of metal ions and the binding distance were also investigated	37 (2015)
2	Evaluation of Anti-inflammatory and Regenerative Efficiency of Naringin and Naringenin in Degenerated Human Nucleus Pulposus Cells: Biological and Molecular Modeling Studies	Molecular docking showed that both naringin and naringenin bind to the selected genes of interest and are identified as potent inhibitors of inflammation used for the treatment of low back pain and sciatica	38 (2019)
3	Molecular docking studies of natural compounds of naringin on enzymes involved in the urea cycle pathway in hyperammonemia	The study reported that naringin interacts with urea cycle enzymes with more hydrogen bonds and higher bonding energy than the standard drug, sodium benzoate. This supports that naringin can prevent experimental hyperammonemia	39 (2020)
4	Evaluation of interaction between citrus flavonoid, naringenin, and pepsin using spectroscopic	The root means square deviation of the naringenin-pepsin complex uncovered an average (1.34 nm) more than that of the free pepsin system (1.33 nm), which	40 (2021)

	analysis and docking simulation	agreed thermal stability and protein structure gain more rigidity. Kinetic studies showed that the activity of the enzyme was decreased	
5	Docking study of naringin binding with COVID-19 main protease enzyme	NAR inhibits the covid 19 protease enzyme better than other flavonoid quercetin, hesperetin, garcina, and naringenin	41 (2021)
6	Network Pharmacology Integrated with Molecular Docking Explores the Mechanisms of Naringin against Osteoporotic Fracture by Regulating Oxidative Stress	Naringin may treat osteoporotic fracture by regulating numerous signaling pathways and targets related to oxidative stress and osteoclast differentiation. These results will provide a theoretical basis for the treatment of osteoporotic fracture	42 (2021)

Future Prospective: In different studies, Naringin has been shown to reduce modern-daydiseases; diabetes, cancer, inflammation, *etc*. in various animal model systems. Its antioxidative property leads to the reduction in oxidative stress-mediated pathogenesis. However, in the context of the effect of Naringin on humans, no epidemiological study has been performed except for a linkage between citrus fruits and a lower rate in breast cancer patients. Naringin has been shown to reduce the development of diabetes and help prevent cancer in diabetic patients.

Based on the experienced gain from different studies, it could be safely concluded that Naringin may potentiate the outcome of radiotherapy by overcoming the radio-diminished immune response and giving a better clearance of tumor by activating the host cytotoxic immune response. Besides, Naringin may also reduce the damage to the normal cells during radiotherapy due to its differential effects on the normal and cancer cells.

CONCLUSION: Naringin is a citrus Flavonoid extracted from a grapefruit peel, Pomelo, Orange, Lemon, *etc*. It can be extracted from powder, not juice, due to higher flavonoid concentrations. As a common waste product, its usage for future work would likely be economical and reduce food waste.

For the analytical study, HPTLC, LC/MS, and HPLC methods were carried out, and have been found that the procedures are simple, rapid, accurate, reproducible, and applicable for the determination of naringin in grapefruit. From various pre-clinical reports, there is self-evident strength of Naringin in applications that deal with bone diseases or stem cells for osteogenic differentiation. Undeniably, Naringin can rectify various disorders and extend several pharmaceutical approaches.

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CONFLICTS OF INTEREST: Nil

REFERENCE:

1. Chutia D, Tyagi CK and Bhuyan NR: Isolation, characterization, and biological evaluation of ethanolic extract of Ajos sacha in Streptozotocin-induced hyperglycemia in Wistar albino rats. South African Journal of Botany 2022; 148: 526-36.
2. Jajo H and Ghosh R: Hepatoprotective activity of the whole plant of *Neptunia prostrata* L. in carbon tetrachloride-induced rats. Int J Curr Pharm Res 2021; 13(6): 56-59.
3. Ghosh R, Jajo H and Acharya PC: An Overview of Neptuniaprostrata: A Source of Herbal Medicine of Ethnopharmacological Importance. Glob J Pharmaceu Sci 2017; 2(1): 555577. DOI: 10.19080/GJPPS.2017.02.555577.
4. Suseem SR and Joseph D: The Myth and the fact on Naringin-A Review. Res J Pharm Technol 2019; 12(1): 367-74.
5. Bharti S, Rani N, Krishnamurthy B and Arya DS: Preclinical evidence for the pharmacological actions of naringin: a review. Planta Medica 2014; 80(06): 437-51.
6. Vishnu Varthan VJ, Srividya AR and Sathish Kumar MN: Role of naringin and naringenin in various diseased conditions-a review. Int J Pharm Res Scholars 2.4 2013; 198-212.
7. Ho PC, Saville DJ, Coville PF and Wanwimolruk S: Content of CYP3A4 inhibitors, naringin, naringenin and bergapten in grapefruit and grapefruit juice products. Pharmaceutica Acta Helvetiae 2000; 74(4): 379-85.
8. Alam MA, Subhan N, Rahman MM, Uddin SJ, Reza HM and Sarker SD: Effect of citrus flavonoids, naringin and naringenin, on metabolic syndrome and their mechanisms of action. Advances in Nutrition 2014; 5(4): 404-17.
9. Ribeiro MH: Naringinases: occurrence, characteristics, and applications. Applied Microbiology and Biotechnology 2011; 90(6): 1883-95.
10. Giannuzzo AN, Boggetti HJ, Nazareno MA and Mishima HT: Supercritical fluid extraction of naringin from the peel of Citrus paradisi. Phytoche Analysis 2003; 14(4): 221-3.
11. Arun Kumar Gupta, Poonam Mishra, Mukut Senapati and Partha Pratim Sahu: A novel electrochemical device for naringin quantification and removal from bitter variety of citrus fruits. Journal of Food Engineering 2021; 306.

12. Jane JL: Starch: structure and properties. Chemical and Functional Properties of Food Saccharides 2004; 82-96.
13. Ioannou I, M'hiri N, Chaaban H, Boudhrioua NM and Ghoul M: Effect of the process, temperature, light and oxygen on naringin extraction and the evolution of its antioxidant activity. Int J Food Sci Technol 2018; 53(12): 2754-60.
14. Nogata Y, Sakamoto K, Shiratsuchi H, Ishii T, Yano M and Ohta H: Flavonoid composition of fruit tissues of citrus species. Bioscience Biotechnology and Biochemistry 2006; 70(1): 178-92.
15. Victor MM, David JM, Sakukuma MC, França EL and Nunes AV: A simple and efficient process for the extraction of naringin from grapefruit peel waste. Green Processing and Synthesis 2018; 7(6): 524-9.
16. Hakim A, Loka IN and Prastiwi NW: New Method for Isolation of Naringin Compound from *Citrus maxima*. Natural Resources 2019 Aug 22; 10(08): 299.
17. Chang CW, Hsiu SL, Wu PP, Kuo SC, Chao PD: HPLC Assays of naringin and hesperidin in chinese herbs and serum. J Food Drug Anal 1997; 5(2).
18. Ding L, Luo X, Tang F, Yuan J, Liu Q and Yao S: Simultaneous determination of flavonoid and alkaloid compounds in Citrus herbs by high-performance liquid chromatography–photodiode array detection–electrospray mass spectrometry. J Chromatogr B 2007; 857(2): 202-9.
19. Kanaze FI, Gabrieli C, Kokkalou E, Georgarakis M and Niopas I: Simultaneous reversed-phase high-performance liquid chromatographic method for the determination of diosmin, hesperidin and naringin in different citrus fruit juices and pharmaceutical formulations. J Pharma Biomed Anal 2003; 33(2): 243-9.
20. Bartella L, Furia E and Di Donna L: Mass spectrometry and potentiometry studies of Al (III)–naringin complexes. RSC Advances 2017; 7(87): 55264-8.
21. Ishii K, Furuta T and Kasuya Y: Mass spectrometric identification and high-performance liquid chromatographic determination of a flavonoid glycoside naringin in human urine. J Agric Food Chem 2000; 48(1): 56-9.
22. Fang T, Wang Y, Ma Y, Su W, Bai Y and Zhao P: A rapid LC/MS/MS quantitation assay for naringin and its two metabolites in rats' plasma. J Pharma Biomed Anal 2006; 40(2): 454-9.
23. Rouseff RL: Liquid chromatographic determination of naringin and neohesperidin as a detector of grapefruit juice in orange juice. J Assoc Off Anal Chem 1988; 71(4): 798-802.
24. Li X, Xiao H, Liang X, Shi D and Liu J: LC–MS/MS determination of naringin, hesperidin and neohesperidin in rat serum after orally administrating the decoction of Bulpleurumfalcatum L. and Fractusaurantii. J Pharma Biomed Anal 2004; 34(1): 159-66.
25. Kranti P. Musmade, M. Trilok, Swapnil J. Dengale, Krishnamurthy Bhat, MS. Reddy, Prashant B. Musmade and N. Udupa: Development and Validation of Liquid Chromatographic Method for Estimation of Naringin in Nanoformulation" Journal ofPharmaceutics2014, Article ID 864901 https://doi.org/10.1155/2014/864901
26. Tong L, Zhou D, Gao J, Zhu Y, Sun H and Bi K: Simultaneous determination of naringin, hesperidin, neohesperidin, naringenin and hesperetin of Fractusaurantii extract in rat plasma by liquid chromatography tandem mass spectrometry. J Pharma Biomed Anal 2012; 58: 58-64.
27. Arnao MB, Casas JL, Del Rio JA, Acosta M and Garcia-Canovas F: An enzymatic colorimetric method for measuring naringin using 2, 2′-azino-bis-(3-ethylbenzthiazoline-6-sulfonic acid) (ABTS) in the presence of peroxidase. Analytical Biochemistry 1990; 185(2): 335-8.
28. Fisher JF and Wheaton TA: A high-pressure liquid chromatographic method for the resolution and quantitation of naringin and naringenin rutinoside in grapefruit juice. J Agric Food Chem 1976; 24(4): 898-9.
29. Ni H, Zhang SF, Gao QF, Hu Y, Jiang ZD and Chen F: Development and evaluation of simultaneous quantification of naringin, prunin, naringenin and limon in in citrus juice. Food Science and Biotechnology 2015; 24(4): 1239-47.
30. Caccamese S and Chillemi R: Racemization at C-2 of naringin in pummelo (Citrus grandis) with increasing maturity determined by chiral high-performance liquid chromatography. J Chromatogr A 2010; 1217(7): 1089-93.
31. Ahmed OM, Mahmoud AM, Abdel-Moneim A and Ashour MB: Antidiabetic effects of hesperidin and naringin in type 2 diabetic rats. Diabetologiacroatica 2012; 41(2).
32. Chen R, Qi QL, Wang MT and Li QY: Therapeutic potential of naringin: an overview. Pharmaceutical biology 2016; 54(12): 3203-10.
33. Ahmed S, Khan H, Aschner M, Hasan MM and Hassan ST: Therapeutic potential of naringin in neurological disorders. Food and Chemical Toxicology 2019; 132: 110646.
34. Den Hartogh DJ and Tsiani E: Antidiabetic properties of naringenin: A citrus fruit polyphenol. Biomolecules 2019; 9(3): 99.
35. Rivoira MA, Rodriguez V, Talamoni G and de Talamoni NT: New perspectives in the pharmacological potential of naringin in medicine. Current Medicinal Chemistry 2021; 28(10): 1987-2007.
36. Ahmed OM, Hassan MA, Abdel-Twab SM and Azeem MN: Navel orange peel hydroethanolic extract, naringin and naringenin have anti-diabetic potentials in type 2 diabetic rats. Biomedicine & Pharmacotherapy 2017; 94: 197-205.
37. Tu B, Wang Y, Mi R, Ouyang Y and Hu YJ: Evaluation of the interaction between naringenin and human serum albumin: Insights from fluorescence spectroscopy, electrochemical measurement and molecular docking. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy 2015; 149: 536-43.
38. Devraj VM, Vemuri SK, Banala RR, Gunda SK, Av GR and Gpv S: Evaluation of anti-inflammatory and regenerative efficiency of naringin and naringenin in degenerated human nucleus pulposus cells: biological and molecular modeling studies. Asian Spine J 2019; 13(6): 875.
39. Arumugam R, Mani R, Venkatesan A, Sengamalai S, Natesan V and Kim SJ: Molecular docking studies of natural compounds of naringin on enzymes involved in the urea cycle pathway in hyperammonemia. Trop J Pharm Res 2020; 19(5): 1037-43.
40. Raeessi-Babaheydari E, Farhadian S and Shareghi B: Evaluation of interaction between citrus flavonoid, naringenin, and pepsin using spectroscopic analysis and docking simulation. J Mol Liq 2021; 339: 116763.
41. Huseen NH: Docking study of naringin binding with COVID-19 main protease enzyme. Iraqi J Pharm Sci 2020; 29(2): 231-8.
42. Yu X, Zhang P, Tang K, Shen G, Chen H, Zhang Z, Zhao W, Shang Q, Zhu G, Tan R and Gan Y: Network pharmacology integrated with molecular docking explores

the mechanisms of naringin against osteoporotic fracture by regulating oxidative stress. Evidence-Based Complementary and Alternative Medicine 2021; 6421122.

43. Venkateswara Rao P, Kiran SD, Rohini P and Bhagyasree P: Flavonoid: A review on Naringenin. J Pharmacogn Phytochem 2017; 6: 2778-83.

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