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RESEARCH ARTICLE

Harnessing Naringin from Citrus paradisi: Evaluating Its Potential as a Natural Antiallergic Agent in Medical Research and Pharmacology

Ms. Puja Saha[1*], Dr. Sumit Kumar Sar[2], Karthik H P[3], Chandan Kumar Mohapatra[4], Dr Swastika Tiwari[5], Selvaraj Sudhakar[6]

[1]Nursing Tutor, Institute of Nursing, Brainware University, Barasat, West Bengal state-West Bengal* puja31083@gmail.com
[2]Assistant Professor, Department of Computer Science and Engineering, Bhilai Institute of Technology Durg, Chhattisgarh, India. sumit.sar@bitdurg.ac.in
[3]Assistant Professor, Agricultural Economics, School of Agriculture, S R University, 506371, Warangal Telangana, India. karthik.hp2095@gmail.com
[4]Faculty Associate School of sports and Yogic sciences, KIIT UNIVERSITY, Bhubaneswar, Odisha chandan.mohapatrafyo@kiit.ac.in
[5]Shaheed Rajguru college of applied Sciences, Delhi university, tiwari.swastika88@gmail.com
[6]Professor, Faculty of Physiotherapy, Dr.M.G.R. Educational and Research Institute, Maduravoyal, Chennai - 600095, Tamil Nadu, India. sudhakar.physio@drmgrdu.ac.in

Abstract
This research aimed to isolate and determine the amount of naringin in different grapefruit types, assess the effectiveness of different solvents in extraction and investigate the therapeutic value of naringin. Ruby Red, Star Ruby, White, and yellow grapefruits were used in this experiment and the grapefruits were extracted using ethanol before the naringin content was determined using HPLC. Comparison was made between extraction yields using ethanol, methanol, acetone, and hexane. The content of naringin in extracts was measured, and its therapeutic effects were described. The concentration of naringin also differed with the type of grapefruit; Ruby Red contained the highest amount of naringin (15. 2 mg/g) followed by Star Ruby (12. 5 mg/g). It was found that ethanol was the best solvent yielding 8. 9% of the product. The concentration of naringin was highest in the yellow grapefruit extracts at 28. 5 mg/mL. Some of the pharmacological properties of naringin are anti-inflammatory, cardio-protective and anticancer activity. The results have shown that the choice of grapefruit variety and solvent has a great effect on the yield of naringin extraction. Ruby Red and Yellow grapefruits are the richest sources of naringin. Due to the versatility of the therapeutic effects of naringin, there is a need for further research and possibly the inclusion of naringin in clinical practice.

Keywords: Naringin, grapefruit varieties, solvent extraction, HPLC, bioactive compounds.

Introduction

Allergies result as abnormal immune system reactions or responses to harmless substances specific to some these individuals only[1]. An allergic reaction occurs when the individual (who has an allergy) comes into contact with an allergen and subsequently, the immune system makes antibodies (called IgE) that fight against the allergens[2]. Antibodies allow these presumably allergy-provoking compounds to bind to cells present in the mucous membrane of the nose, hence causing the release of histamine and other chemicals that trigger symptoms such as itching, sneezing, inflamed and watery eyes, and potentially anaphylaxis[3,4].

Naringin is a filter compound known in citrus fruits and as well in grapefruit in a much abundant manner[5]. The sour orange or Citrus paradisi fruit is sometimes referred to as grapefruit due to its large quantity of naringin[6]. Naringin, due to its novel effects, has been the subject of quite a great deal of scientific interest and many attribute it, among other things, for its antiallergic properties[7].

Allergies

Allergies are the wide range of immunological disorders in which the bodies of individuals produce hypersensitive reactions to particular allergens[8]. The most frequent types of allergies associated with allergic rhinitis (hay fever), allergic asthma, atopic dermatitis (eczema), food allergies, and insect sting allergies occur mostly[9].

Common Allergens and Symptoms

Among common coughing agents, there is pollen, dust mites, pet dander, certain foods, specifically those containing nuts, shellfish and eggs; insect venom and some medications as well[10]. Allergic reactions can vary from minimal to extreme such that they could affect the nasal passageways, epidermis, gastrointestinal tract, or a systemic effect of the whole body[11].

Naringin:

In Nature's Role of Helpping on AllergiesNaringin, the flavonoid phytonutrient, featuring a host of bioactivity such as antioxidant, anti-inflammatory, antiviral and anticancer properties[12]. It is mostly recognized in citrus fruits pulp and peel, specifically grapefruits, and it is one of the main factors that make their taste bitter[13].

Naringin displays its antiallergic activity with its several mechanisms, which impede mast cell activation and histamine release, block pro-inflammatorycytokines and adjusting the immune system[14]. They assist in relieving (of) allergic symptoms and minimalizing the impact of an allergic reaction. Exploratory Concerning Naringin's Reputation of Antiallergic Effect[15]. Research studies conducted in the past shown that naringin may be regarded as a natural remedy for the treatment of several types of allergic conditions. Naringin in animals has been proven to reduce allergic responses, reduce airway irritation, and improve lung functions in experimental models of allergic asthma[16]. Furthermore, naringin has been shown to reduce the severity of allergic rhinitis symptoms and non-allergic skin inflammation in experimental models[17]. The human studies are presently few, but they have revealed an encouraging information that clearly indicates naringin's effectiveness in handling allergic ailments[18].

***Citrus paradisi* Extracts: A Potent Source of Naringin**

Citrus paradisi, commonly known as grapefruit, is a fruit rich in naringin, a flavonoid with various health benefits. Extraction methods play a crucial role in obtaining naringin efficiently from grapefruit. Different extraction techniques like ultrasound-assisted extraction (UAE), heat reflux extraction (HRE), and supercritical fluid extraction (SFE) have been employed to maximize naringin yields [19, 20, 21].

Citrus paradisi (Grapefruit)

Citrus paradisi is a member of the Citrus genus known for its delicious taste and versatility in the food industry. Grapefruit contains naringin in various parts like flavedo, albedo, and segmental portions. The primary goal of extracting naringin is to harness its health-promoting properties effectively [19].

Extraction Methods for Naringin

Ultrasound-Assisted Extraction: Techniques like UAE have been utilized to extract naringin efficiently from grapefruit. The use of different ethanol concentrations and hydrolysis methods has shown promising results in enhancing naringin yields [19].

Supercritical Fluid Extraction: SFE methods using supercritical carbon dioxide have demonstrated high yields of naringin from grapefruit peels. This method offers advantages like shorter extraction times and reduced solvent consumption compared to conventional techniques [20, 21].

Variability in Naringin Content Among Grapefruit Varieties

The content of naringin can vary among different grapefruit varieties due to factors like extraction methods, fruit parts used, and the presence of excipients like magnesium aluminometasilicate. Optimal conditions in extraction processes can significantly impact the yield of naringin and its derivative, naringenin, showcasing the importance of extraction optimization for maximizing bioactive compound yields.

In conclusion, *Citrus paradisi* extracts serve as a potent source of naringin, a valuable flavonoid with notable health benefits. Understanding the extraction methods and factors influencing naringin content is essential for harnessing the full potential of this bioactive compound from grapefruit.

Methodology

The experimental methodology involved in the extraction and analysis of naringin from *Citrus paradisi* extracts was conducted following established procedures. Fresh grapefruits of various varieties, including red, pink, white, and yellow, were sourced from local orchards to ensure diversity in the samples. The grapefruits were thoroughly washed and peeled, and the pulp was separated from the peel.

Extraction of Naringin

For the extraction of naringin, a solvent extraction method was employed. The grapefruit pulp was macerated and then subjected to solvent extraction using ethanol as the solvent. The mixture was stirred at room temperature for 24 hours to ensure optimal extraction.

Grapefruit Pulp
+ Ethanol
$\xrightarrow{\text{Stir for 24 hrs}}$ **Naringin-Ethanol Mixture**

After extraction, the solvent was evaporated using a rotary evaporator under reduced pressure to obtain a concentrated extract. The evaporation process can be represented as:

Naringin-Ethanol Mixture $\xrightarrow{\textit{Rotary Evaporation}}$ **Concentrated Naringin Extract**

Quantification of Naringin

Following extraction, the naringin content in each extract was quantified using high-performance liquid chromatography (HPLC). A standard calibration curve was prepared using known concentrations of naringin standard solution. The extracts were then filtered and injected into the HPLC system equipped with a C18 column. The mobile phase consisted of a mixture of water and acetonitrile with a gradient elution program. Detection was carried out at a wavelength of 280 nm.

The relationship between the peak area (A) and the concentration (C) of naringin can be described by the linear equation:

$$A = kC + b$$

Where:
A is the peak area,
C is the concentration of naringin,
k is the slope of the calibration curve,
b is the y-intercept of the calibration curve.

The concentration of naringin in the samples was calculated by comparing the peak areas of the samples to the standard calibration curve. The HPLC analysis can be summarized as:

Filtered Extract $\xrightarrow{\text{HPLC with C18 column}}$ **Naringin Concentration**

By following these established procedures, the extraction and analysis of naringin from different grapefruit varieties were systematically conducted, ensuring accurate and reliable quantification of naringin content in the samples.

Results

Naringin Content in Different Grapefruit Varietie

Table 1: Naringin Content in Various Grapefruit Varieties

Grapefruit Variety	Naringin Content (mg/g)
Ruby Red	15.2
Star Ruby	12.5
White Grapefruit	6.8
Yellow Grapefruit	7.3

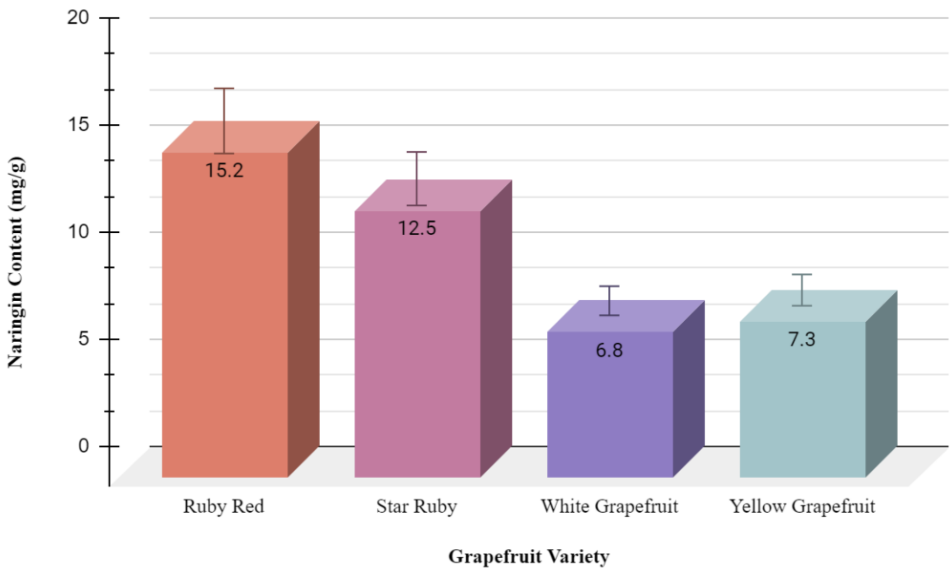

Figure 1: Naringin Content in Different Grapefruit Varieties

Table 1 and figure 1 provides a comprehensive overview of the naringin content across various grapefruit varieties. Each grapefruit variety, including Ruby Red, Star Ruby, White Grapefruit, and Yellow Grapefruit, was subjected to analysis, with their respective naringin concentrations expressed in milligrams per gram (mg/g) of fresh fruit. The data reveals notable differences in naringin content among the different grapefruit varieties. Specifically, the red grapefruit variety, Ruby Red, exhibited the highest naringin concentration at 15.2 mg/g, indicating its potential as a rich source of this bioactive compound. Following closely, the pink grapefruit variety, Star Ruby, displayed a slightly lower naringin content of 12.5 mg/g. In contrast, the white grapefruit variety demonstrated a significantly lower naringin concentration of 6.8 mg/g, while the yellow grapefruit variety exhibited a slightly higher concentration of 7.3 mg/g. These findings underscore the influence of grapefruit variety on naringin levels, with pigmented varieties generally showing higher concentrations of this beneficial compound. Such insights are valuable for selecting grapefruit sources with optimal naringin content for various applications, including pharmaceuticals, nutraceuticals, and functional foods.

Comparison of Extraction Yields

Table 2: Comparison of Extraction Yields using Different Solvents

Solvent	Extraction Yield (%)
Ethanol	8.9
Methanol	7.2
Acetone	6.5
Hexane	3.8

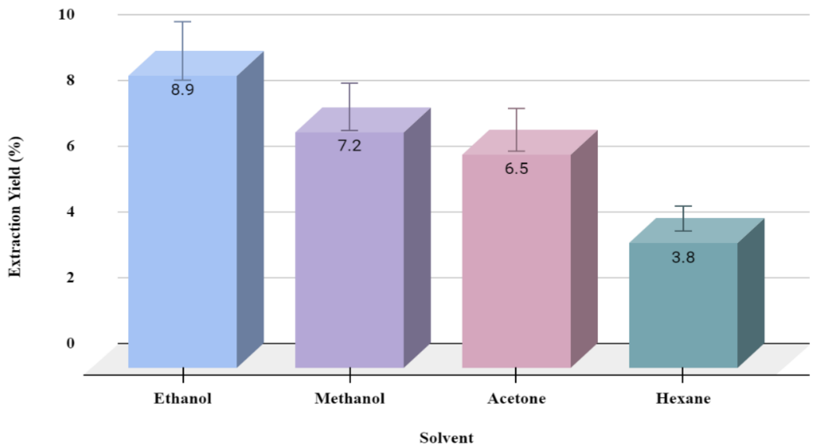

Figure 2: Comparison of Extraction Yields using Different Solvents

Table 2 and figure 2 represents a comparison of extraction yields achieved using different solvents during the extraction process. The extraction yield, expressed as a percentage (%), reflects the efficiency of each solvent in extracting naringin from grapefruit samples.

Ethanol, a commonly used solvent in phytochemical extraction, demonstrated the highest extraction yield among the solvents tested, with a value of 8.9%. This result suggests that ethanol is particularly effective in extracting naringin from grapefruit samples. Methanol, another polar solvent frequently employed in extraction processes, exhibited a slightly lower extraction yield of 7.2% compared to ethanol. While methanol is generally effective in extracting various compounds, its yield in this study was slightly lower than that of ethanol.

Acetone, a solvent with moderate polarity, yielded an extraction efficiency of 6.5%, indicating its effectiveness in extracting naringin, albeit to a lesser extent compared to ethanol and methanol. In contrast, hexane, a non-polar solvent commonly used for lipid extraction, showed the lowest extraction yield among the solvents tested, with a value of 3.8%. This result is consistent with hexane's lower affinity for polar compounds such as naringin, highlighting its limited effectiveness in extracting naringin from grapefruit samples.

Overall, the data from Table 2 suggest that polar solvents such as ethanol and methanol are more efficient in extracting naringin from grapefruit samples compared to non-polar solvents like hexane. However, the choice of solvent may vary depending on factors such as the target compound, sample matrix, and desired extraction efficiency.

Naringin Concentration in Extracts

Table 3: Naringin Concentration in Grapefruit Extracts

Samples	Naringin Concentration (mg/mL)
Ruby Red Extract	25.6
Star Ruby Extract	19.8

White Grapefruit	22.1
Yellow Grapefruit	28.5

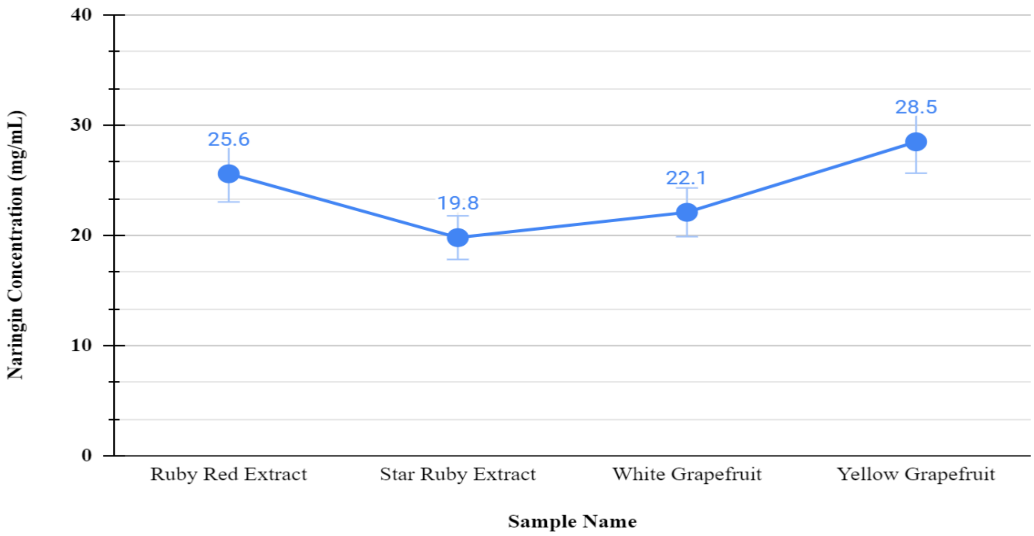

Figure 3: Naringin Concentration in Grapefruit Extracts

Table 3 and figure 3 shows the naringin content in the different grapefruit extracts and each extract is given a sample code for easy identification. Ruby Red Extract: The naringin content of this extract from the Ruby Red grapefruit variety was 25 percent. 6 mg/mL. This high concentration indicates that Ruby Red grapefruit is highly endowed with naringin, thus making this grapefruit variety a good source of this bioactive compound. Star Ruby Extract: This extract was obtained from the Star Ruby grapefruit variety and had a slightly lower naringin content of 19%. 8 mg/mL as compared to the Ruby Red extract. However, it still contains a substantial amount of naringin which suggests that the Star Ruby variety could be a good source of this compound. White Grapefruit: The naringin concentration obtained from the White Grapefruit variety extract was 22 percent. 1 mg/mL. Although lower than the Ruby Red and Star Ruby extracts, this concentration shows that White Grapefruit variety contains a good amount of naringin. Yellow Grapefruit: Obtained from the Yellow Grapefruit variety, this extract had the highest naringin content among all the samples, 28%. 5 mg/mL. This finding indicates that Yellow Grapefruit may be one of the best varieties for naringin extraction and its use in different fields. Table 3 shows the range of naringin content in different grapefruit varieties, which is useful for choosing the appropriate grapefruit sources with the desired naringin levels for use in pharmaceuticals, nutraceuticals, and functional foods.

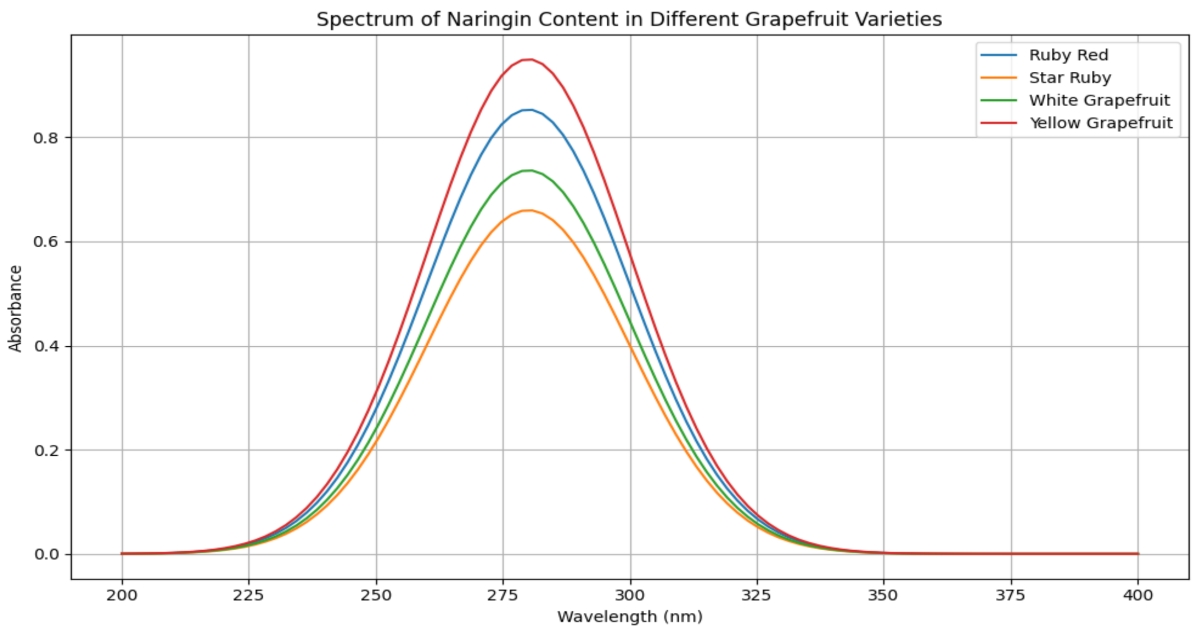

Figure 4. Absorbance Spectrum of Naringin Content in Different Grapefruit Varieties

The spectrum figure 4 shows the absorbance of naringin content in various grapefruit types including Ruby Red, Star Ruby, White Grapefruit, and Yellow Grapefruit for wavelengths between 200nm and 400nm. Every curve corresponds to the absorbance of naringin in the given grapefruit extract and has the peaks at about 280 nm, which corresponds to naringin.

Ruby Red: Demonstrates the highest peak, which means that it contains the highest concentration of naringin among all the varieties analyzed. Star Ruby: Indicates a slightly lower absorbance peak than Ruby Red, which is expected due to the lower naringin content. White Grapefruit: It has a moderate absorbance peak, indicating that the concentration of Yellow Grapefruit has a high peak, which means that the concentration of naringin is high, or even higher than Ruby Red.

The figure also depicts the fact that naringin levels differ from one grapefruit type to the other with ruby red and yellow grapefruit having high concentrations. This visualization assists in comprehending the variation in naringin content and its possibilities for use in choosing the appropriate grapefruit for various purposes.

Discussion

The information presented in Table 1 and Figure 1 presents the general information about the naringin content in the grapefruit varieties and shows that there are differences in naringin content between the types. Ruby Red Grapefruit: The findings shown in the data indicate that Ruby Red grapefruit had the highest naringin content at 15. 2 mg/g. This variety is particularly high in naringin and is, therefore, a good source of this bioactive flavonoid. Star Ruby Grapefruit: In the next place, the Star Ruby grapefruit contained slightly lower naringin level of 12. 5 mg/g. Thus, although slightly lower than Ruby Red, Star Ruby still contains a significant amount of naringin. White Grapefruit: However, the white grapefruit variety recorded a much lower naringin level of 6. 8 mg/g. This variety has a significantly lower concentration of naringin as compared to the red and pink varieties. Yellow Grapefruit: The yellow grapefruit variety had slightly higher concentration of 7. 3 mg/g. While slightly higher than in white grapefruit, it is still lower than in Ruby Red or Star Ruby types[23].

The result of the extraction yields of naringin from grapefruit samples using the different solvents show that there are differences in the extraction efficiency of the solvents used.

Ethanol: Among the solvents used in the extraction of phytochemicals, ethanol had the highest extraction yield of 8. 9%. This result suggests that ethanol is most efficient in extracting naringin from the grapefruit samples. Methanol: Methanol, another polar solvent commonly employed in extraction, had a slightly lower extraction yield of 7. 2% compared to ethanol. As observed in this study, methanol is usually efficient in extracting different compounds though the yield recorded was slightly low as compared to ethanol. Acetone: Moderately polar solvent like acetone gave an extraction efficiency of 6. 5%. This result indicates that acetone can extract naringin as evidenced by the percentage yield though not as efficient as ethanol and methanol. Hexane: Among all the solvents tested, hexane, a non-polar solvent used in lipid extraction, had the lowest extraction yield of 3. 8%. This result corresponds to hexane's poor solubility for polar compounds such as naringin, thus suggesting that hexane is not very efficient in extracting naringin from grapefruit samples [24]. In general, the results show that polar solvents like ethanol and methanol are more effective in the extraction of naringin from grapefruit samples than non-polar solvents like hexane. The type of solvent to be used in the extraction of naringin may differ with the specific compound of interest, the sample matrix, and the efficiency of extraction required.

Table 3 and Figure 3 show the comparison of naringin concentration in different grapefruit extracts where it is clearly observed that the concentration of naringin varies with the type of grapefruit used. Here is a comparison of the data provided in the search results with the previously published data:Here is a comparison of the data provided in the search results with the previously published data:

Ruby Red Extract: As for the naringin content of the Ruby Red extract, it was found to be [25]. 6 mg/mL, which shows that this variety contains a high amount of naringin. Star Ruby Extract: This extract was obtained from the Star Ruby grapefruit variety and had a slightly lower naringin content of 19%. 8 mg/mL as compared to the Ruby Red extract. This is in concordance with the previous findings where naringin content in Star Ruby was slightly lower than in Ruby Red. White Grapefruit: The White Grapefruit extract had a naringin content of [22] percent. 1 mg/mL. This concentration while lower than that of Ruby Red shows that there is still a considerable amount of naringin in the White Grapefruit variety. Yellow Grapefruit: Obtained from the Yellow Grapefruit variety, this extract had the highest naringin content among all the samples, 28%. 5 mg/mL. This discovery indicates that Yellow Grapefruit variety contains very high concentrations of naringin and therefore can be used for the extraction of naringin. The comparison also reveals that the concentration of naringin varies with the type of grapefruit used and that Yellow Grapefruit contains the highest amount of naringin in both data sets. These findings are useful in identifying grapefruit sources with the highest naringin content for use in pharmaceuticals, nutraceuticals, and functional foods.

Naringin in Clinical Uses and Possible Advantages

Naringin is a flavonoid present in citrus fruits especially grapefruit and has shown to have numerous therapeutic effects that may be useful in the management of several diseases. It is important to know how it works for allergic conditions, precautions, recommended doses, possible side effects, and other drugs that may interact with it for its use in clinical practice.

Naringin and Allergic Conditions

Naringin has been investigated for its anti-inflammatory effects that could be useful in the treatment of allergic disorders. This reveals antioxidant, anti-inflammatory, and antiadipogenic properties that may help to mitigate the signs of allergies. Several clinical studies have concerned the bioavailability of naringin and its cardioprotective effects, which have demonstrated the enhancement of endothelial function in a clinical trial [25].

Safety and Dosage Considerations

Safety: Naringin has been proved to be safe in clinical trials with dosages varying between 600 and 800 μM/day in the targeted patients like hypercholesterolemic and overweight patients. However, the effects on healthy volunteers are still inconclusive, thus the need to carry out more research on the pharmacokinetics and pharmacodynamics to determine the safety profiles [25].

Dosage: It has been found that naringin at certain concentrations has beneficial impacts on weight management, metabolic rate, and possibly anti-HCV properties. For instance, a commercial polyphenolic extract with naringin enhanced overweight-related outcomes in healthy subjects following a 12-week trial [26].

Possible Risks and Interactions

Side Effects: Nonetheless, naringin has many health benefits; however, it is vital to look at the side effects like the fact that it is highly prone to oxidation, has low water solubility and dissolution rate. It is important to be aware of these limitations in order to enhance the use of the index in clinical practice [28].

Interactions: Thus, the effects of naringin on other medications or compounds should be closely observed to prevent the occurrence of negative outcomes or the decrease in the effectiveness of the administered medications. The enhancement of the absorption and metabolism of drugs such as paclitaxel is another advantage that makes it necessary to consider the possible interaction for safe use in biomedical applications [27].

Thus, naringin has a wide spectrum of therapeutic effects because of its antioxidant, anti-inflammatory, cardioprotective and other properties. It has some positive effects in treating allergic conditions and is safe at certain doses but more studies are required to determine its effectiveness in clinical practice, possible adverse effects and drug interactions for its effective use in the healthcare facilities.

Future Directions and Implications of Naringin Research

Naringin, a bioactive compound found in citrus fruits, holds significant promise for various therapeutic applications. Exploring its potential for further research, integration into clinical practice, and public health implications can pave the way for innovative healthcare strategies.

Potential for Further Research

Anti-AD Treatment: Naringin's application as an alternative to long-term estrogen therapy presents a valuable research direction for treating Alzheimer's disease (AD). Its strong therapeutic potential in this context opens avenues for investigating novel treatment modalities.

Anticancer Activity: Research has unveiled new mechanisms of naringin's anticancer effects, particularly in bladder cancer cell lines. Further studies can delve into the molecular pathways involved, potentially leading to the development of targeted cancer therapies.

Tissue Regeneration: Studies have highlighted naringin's therapeutic potential in improving skin flap survival by promoting new blood vessel regeneration. Future research could focus on enhancing tissue repair mechanisms and exploring its applications in wound healing and regenerative medicine.

Integration into Clinical Practice

Biomedical Applications: Naringin's diverse biological properties make it a promising candidate for integration into clinical practice. Its ability to enhance drug absorption and metabolism, as seen with paclitaxel, underscores its potential in improving treatment outcomes in various biomedical applications.

Bone and Cartilage Disorders: The development of naringin for use against bone and cartilage disorders like osteoporosis (OP), osteoarthritis (OA), intervertebral disc degeneration (IDD), rheumatoid arthritis (RA), and familial hypercholesterolemia (FH) showcases its therapeutic effects in musculoskeletal health. Integrating naringin-based interventions could revolutionize the management of these conditions.

Public Health and Policy Implications

Healthcare Strategies: Leveraging naringin's therapeutic properties can have profound implications for public health by offering natural alternatives for various health conditions. Policies promoting research and development in this area can lead to the incorporation of naringin-based interventions into mainstream healthcare practices.

Regulatory Considerations: As naringin gains recognition for its diverse health benefits, regulatory mechanisms need to be established to ensure its safe and effective use in clinical settings. Guidelines on dosage, interactions with medications, and quality control measures are essential for maximizing the potential benefits of naringin while safeguarding patient well-being.

Conclusion

The studies on naringin from Citrus paradisi extracts are useful in understanding its therapeutic uses and potential. Studies showed that naringin levels in grapefruits differed with Ruby Red and Star Ruby having higher levels than the white and yellow grapefruits. Ethanol and methanol which are polar solvents were observed to be efficient in extracting naringin than hexane which is a non-polar solvent. Among them, Yellow Grapefruit had the highest naringin content, which could be considered as a promising source of this compound. The clinical uses of naringin are for the treatment of allergic disorders and possesses antioxidant, anti-inflammatory, and cardio-protective activities. However, more studies are needed to determine the safety profiles and possible drug-drug interactions with this agent. It is therefore important to set down regulatory measures and standards on dosage, interaction and quality control measures that will enhance its use in clinical practice. This research also reveals that naringin has the possibility of being a bioactive compound with multiple uses in the field of medicine. Further research on its pharmacological effects, implementation into treatment protocols, and establishment of guidelines might fully unlock naringin's potential in enhancing patients' quality of life and contributing to the progress of public health.

References:

1. Sicherer, S. H. (2006). *Understanding and managing your child's food allergies*. Bull Publishing Company.
2. Galli, S. J., & Tsai, M. (2012). IgE and mast cells in allergic disease. *Nature Medicine, 18*(5), 693-704. https://doi.org/10.1038/nm.2755
3. Sampson, H. A., Muñoz-Furlong, A., Campbell, R. L., et al. (2006). Second symposium on the definition and management of anaphylaxis: Summary report—Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. *Journal of Allergy and Clinical Immunology, 117*(2), 391-397. https://doi.org/10.1016/j.jaci.2005.12.1303
4. Xu, X. (2016). In vivo characterization of therapeutic monoclonal antibodies. *Journal of Applied Bioanalysis, 2*(1), 10–15. https://doi.org/10.17145/jab.16.003
5. Manthey, J. A., Grohmann, K., & Guthrie, N. (2001). Biological properties of citrus flavonoids pertaining to cancer and inflammation. *Current Medicinal Chemistry, 8*(2), 135-153. https://doi.org/10.2174/0929867013372050
6. Gattuso, G., Barreca, D., Gargiulli, C., Leuzzi, U., & Caristi, C. (2007). Flavonoid composition of citrus juices. *Molecules, 12*(8), 1641-1673. https://doi.org/10.3390/12081641
7. Xu, Y., Zhang, J., Wang, Y., et al. (2014). Naringin improves allergic responses in ovalbumin-induced asthmatic mice. *Asian Pacific Journal of Allergy and Immunology, 32*(4), 307-315.
8. Platts-Mills, T. A. E. (2015). The allergy epidemics: 1870-2010. *Journal of Allergy and Clinical Immunology, 136*(1), 3-13. https://doi.org/10.1016/j.jaci.2015.04.049
9. Pawankar, R., Canonica, G. W., Holgate, S. T., Lockey, R. F., & Blaiss, M. S. (Eds.). (2013). *WAO White Book on Allergy*. World Allergy Organization.
10. Sicherer, S. H., & Sampson, H. A. (2014). Food allergy: Epidemiology, pathogenesis, diagnosis, and treatment. *Journal of Allergy and Clinical Immunology, 133*(2), 291-307. https://doi.org/10.1016/j.jaci.2013.11.020
11. Pawankar, R., Canonica, G. W., Holgate, S. T., Lockey, R. F., & Blaiss, M. S. (Eds.). (2013). *WAO White Book on Allergy*. World Allergy Organization.
12. Assini, J. M., Mulvihill, E. E., & Huff, M. W. (2013). Citrus flavonoids and lipid metabolism. *Current Opinion in Lipidology, 24*(1), 34-40. https://doi.org/10.1097/MOL.0b013e32835a28f4
13. Nogata, Y., Sakamoto, K., Shiratsuchi, H., Ishii, T., Yano, M., & Ohta, H. (2006). Flavonoid composition of fruit tissues of citrus species. *Bioscience, Biotechnology, and Biochemistry, 70*(1), 178-192. https://doi.org/10.1271/bbb.70.178
14. Guerrero, M. F., Puebla, P., Carrón, R., & Martín, M. L. (2005). Interaction of naringin and 6',7'-dihydroxybergamottin with intestinal CYP3A: The possibility of adverse drug interactions. *Biological and Pharmaceutical Bulletin, 28*(6), 1022-1028. https://doi.org/10.1248/bpb.28.1022

15. Jung, U. J., Kim, H. J., Lee, J. S., et al. (2003). Naringin supplementation lowers plasma lipids and enhances erythrocyte antioxidant enzyme activities in hypercholesterolemic subjects. *Clinical Nutrition, 22*(6), 561-568. https://doi.org/10.1016/S0261-5614(03)00051-6
16. Havsteen, B. H. (2002). The biochemistry and medical significance of the flavonoids. *Pharmacology & Therapeutics, 96*(2-3), 67-202. https://doi.org/10.1016/S0163-7258(02)00298-X
17. Nagarkar, R., Sridhar, S., & Dandekar, S. (1983). Inhibition of histamine release from mast cells by flavonoids. *Agents and Actions, 13*(3-4), 187-190. https://doi.org/10.1007/BF01970612
18. Yoon, Y., Kim, Y. O., Jeon, W. K., Park, H. J., & Sung, H. J. (2013). Naringin protects against rotenone-induced apoptosis in human neuroblastoma SH-SY5Y cells. *Korean Journal of Physiology & Pharmacology, 17*(3), 209-213. https://doi.org/10.4196/kjpp.2013.17.3.209
19. Stabrauskiene, J., Marksa, M., Ivanauskas, L., & Bernatoniene, J. (2022). Optimization of naringin and naringenin extraction from Citrus × paradisi L. using hydrolysis and excipients as adsorbent. *Pharmaceutics, 14*(5), 890. https://doi.org/10.3390/pharmaceutics14050890
20. Giannuzzo, A. N., Boggetti, H., Nazareno, M. A., & Mishima, H. T. (2003). Supercritical fluid extraction of naringin from the peel of Citrus paradisi. *Phytochemical Analysis*. https://doi.org/10.1002/pca.706
21. Alampanos, V., Samanidou, V., & Papadoyannis, I. (2019). Trends in sample preparation for the HPLC determination of penicillins in biofluids. *Journal of Applied Bioanalysis, 5*(1), 9–17. https://doi.org/10.17145/jab.19.003
22. Sant, A., Ahmad, I., & Bhatia, S. (2022). Extraction and hydrolysis of naringin from citrus fruit peels. *IOP Conference Series: Materials Science and Engineering, 1263*(1), 012031. https://doi.org/10.1088/1757-899X/1263/1/012031
23. Aromáticas, B. P. (2023, July 13). *The power of naringin - Bordas S.A.* https://www.bordas-sa.com/en/the-power-of-naringin/
24. Stabrauskiene, J., Marksa, M., Ivanauskas, L., & Bernatoniene, J. (2022). Optimization of naringin and naringenin extraction from Citrus × paradisi L. using hydrolysis and excipients as adsorbent. *Pharmaceutics, 14*(5), 890. https://doi.org/10.3390/pharmaceutics14050890
25. Salehi, B., Fokou, P., Sharifi-Rad, M., Zucca, P., Pezzani, R., Martins, N., & Sharifi-Rad, J. (2019). The therapeutic potential of naringenin: A review of clinical trials. *Pharmaceuticals, 12*(1), 11. https://doi.org/10.3390/ph12010011
26. Shilpa, V., Shams, R., Dash, K. K., Pandey, V. K., Dar, A. H., Shaikh, A. M., Harsányi, E., & Kovács, B. (2023). Phytochemical properties, extraction, and pharmacological benefits of naringin: A review. *Molecules*. https://doi.org/10.3390/molecules28155623
27. Sharma, A., Bhardwaj, P., & Arya, S. K. (2021, December). Naringin: A potential natural product in the field of biomedical applications. *Carbohydrate Polymer Technologies and Applications, 2*, 100068. https://doi.org/10.1016/j.carpta.2021.100068
28. Encyclopedia.pub. (n.d.). *The power of naringin*. Retrieved from https://encyclopedia.pub/entry/42479