Review Article

An insight into the structure and functions of flabelliferins and borassosides: Nutraceuticals in Asian palm (*Borassus flabellifer*)

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Abstract: Palmyraculture is a sustainable livelihood, in which people structure their lifestyle utilizing the values of the palmyra palm. The Asian palmyra palm, *Borassus flabellifer*, gives a lot of nutritional and nutraceutical products, as it is rich in vital biomolecules, especially flabelliferins and borassosides. Flabelliferins are found in the fruit, tuber, and inflorescence of palmyra palm, and the borassosides are found in the inflorescence. There are 14 types of flabelliferins (only nine of their structures are known) and six types of borassosides have been extracted so far. Flabelliferin F-II reduces intestinal glucose uptake and is anti-diabetic and anti-obesitic. Flabelliferin FB is an antimicrobial agent, an inhibitor for SARS-CoV main proteinase, a SARS-CoV main protease, and a human cellular transmembrane serine proteinase, while borassoside E is an antifungal agent. Further studies have to be conducted to determine the structures and functions of the other flabelliferins and borassosides.

Keywords: Asian palm; *Borassus flabellifer*; borassosides; flabelliferins; nutraceuticals; palmyraculture

1. Introduction

Palmyra palm, botanically known as *Borassus flabellifer,* belongs to the family of Palmae and the sub-family of Boracidae[1]. There are five types of plants that belong to the genus Borassus: *Borassus aethiopum*, *Borassus akeassii*, *Borassus flabellifer Linn.*, *Borassus heineanus*, and *Borassus madagascariensis*[2]. Due to the presence of some vital biomolecules, the palmyra palm has a lot of medicinal and nutritional properties. The palmyra palm fruit is a diuretic, antioxidant, antibacterial agent, laxative, wound healer, and immune modulator. It is also used against helminthic and inflammation, and it helps prevent malnutrition[3]. The ripened fruit is rich in vitamins A, B1, B2, B3, B6, C, D3, E, and K and in flabelliferins, tannins, sugars, steroidal saponins, and phenolic compounds[4]. The various parts of the palmyra palm, starting from the fruit, leaves, trunk, sap, etc., have been utilized for generations for food, shelter, and medicinal needs. The lesser-known substances, flabelliferins and borassosides, have now been gaining attention because of their therapeutic potential. As the botanical name suggests, both flabelliferins and borassosides are some of the main biomolecules present in different parts of the palmyra palm tree and are found to be performing significant bioactivities, and thus flabelliferins and borassosides have emerged as promising nutraceuticals, as highlighted in **Figure 1**. They possess distinctive chemical structures and show unique biological activities.

The paper focuses on a general overview of the structural features and functional properties of flabelliferins and borassosides. They are potentially suitable to be effective nutraceuticals based on their chemical properties and molecular structures. Additionally, their extraction and separation methods, biological activities, and scope and challenges when it comes to the pharmaceutical, nutraceutical, and food industries are highlighted.

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Figure 1. Different parts of palmyra tree have flabelliferins and borassosides.

2. Classification and sources

Flabelliferins are biomolecules that belong to the group of steroidal saponins. The name flabelliferin originated from the species name, which is flabellifer. Different types of flabelliferins can be extracted from *Borassus flabellifer* (ripened fruit, tuber, and inflorescence) and the sponge *Cateriospongia flabellifera*[5–8]. In 1994, two flabelliferin molecules were first identified from the fruit pulp of palmyra palm and were named F-I and F-II. From that study, it was found that F-II is the reason for the bitterness of the fruit pulp, while F-I causes less bitterness[9]. Another study has shown that three other types of flabelliferins can be extracted from the palmyra fruit pulp: F_B and F_C flabelliferins (triglycosides) and F_D flabelliferin (diglycoside)[10]. Thus, there are five main types of flabelliferins extracted from the fruit pulp of Palmyra (F-I, F-II, F_B, F_C, and F_D).

Borassosides are spirostane that belong to the group of steroid saponins[11]. These molecules can be extracted from the male inflorescence of *Borassus flabellifer*, the rhizome of *Trillium govanianum*, and *Dracaena marginata*[12–14]. From *Borassus flabellifer*, many substances have been identified, such as borassosides A through borassosides F, uracil, nicotinamide, 2,3,4-trihydroxy-5-methyl acetophenone, and (17)-23-(E)-dammara-20,23-diene-3,25-diol[15].

3. Extraction and separation techniques

There have been different techniques used so far to separate flabelliferins. Selective solvent extraction is used to separate flabelliferins based on the carbohydrate moiety[16]. Thin layer chromatography helps in identifying the varieties of flabelliferins. Medium-pressure liquid chromatography is effective in separating five types of flabelliferins, including F_D, F_E, F_F, and F_N, and this method is found to be cost-effective, time-saving, and efficient and can separate all types of flabelliferins. The direct isolation method is able to separate six types of flabelliferins (F-II, F_B, F_C, F_D, F_E, and F_F)[17]. Also, solvent gradient column chromatography and chromatotron are used for the separation[18].

Additionally, the debittering of the palmyra fruit pulp, as shown in **Figure 2**, can be done by either using the traditional way of heating the fruit pulp or by enzymatic debittering using naringinase (a mixture of β-glucosidase and β-rhamnosidase from *Penicillium decumbens*) or Termamyl (a heat-stable α-amylase extracted from *Bacillus licheniformis*), which can also debitter crude bitter principal extracts (containing flabelliferins I and II). Enzymatic debittering removes the bitter taste by removing F-II. The enzymes are also found to remove the antimicrobial flabelliferin (F_B), which helps in producing two new non-bitter flabelliferins that are present in the roots of the palmyra tree[9,19]. The debittered pulp with naringinase is found to be nutritious and helps in weight gain in mice.

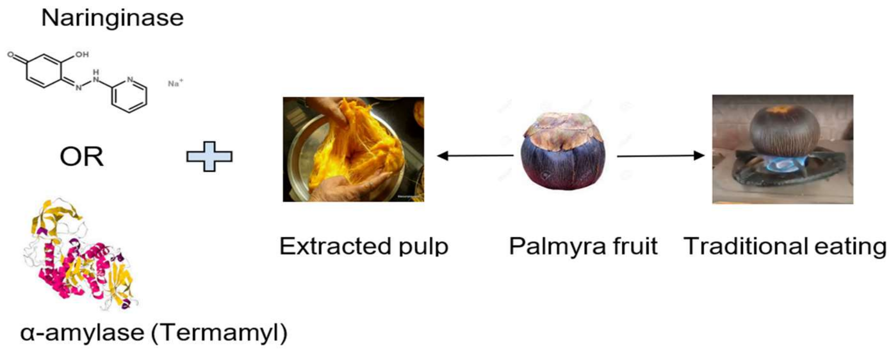

Figure 2. Biochemical and physical debittering processes of Palmyra fruit pulp.

A mix of chromatography technologies and solvent-based extraction procedures is normally used to extract and separate borassosides. The first step is usually dissolving the borassosides or the plant materials that contain them, such as the male inflorescence of *Borassus flabellifer*. They are first macerated or immersed in organic solvents, such as methanol or ethanol[20]. Borassosides are one of a group of different chemicals that are included in the final crude extract.

In order to purify these substances, processes, such as column chromatography, are routinely carried out. Such approaches allow the separation of borassosides based on their distinct features[21]. To get highly pure borassosides for use in research or industry, further chromatographic processes or crystallization may be required.

4. Structural characteristics

All the flabelliferins, as highlighted in **Figure 3**, are found to have β-Sitsosterol as the steroidal component. Only five of the flabelliferin structures have been identified, out of the 14 flabelliferins[18,22].

Flabelliferin II, which is the bitter flabelliferin, is a tetraglycoside having two glucose and two rhamnose residues[9]. From a methylation analysis, it was found that the carbohydrate chain of this molecule is not branched. Flabelliferin B is a branched tetra glycoside having one glucose and two rhamnose residues, and it is the only branched flabelliferin identified so far[18].

The methanolic extract of the male flowers is found to have six types of borassosides (new spirostane-type steroid saponins), which are borassosides A, B, C, D, E, and F[20], as highlighted in **Figure 4**. In rats loaded with sucrose, a methanolic extract from the male flowers of *Borassus flabellifer* was observed to prevent an increase in serum glucose levels.

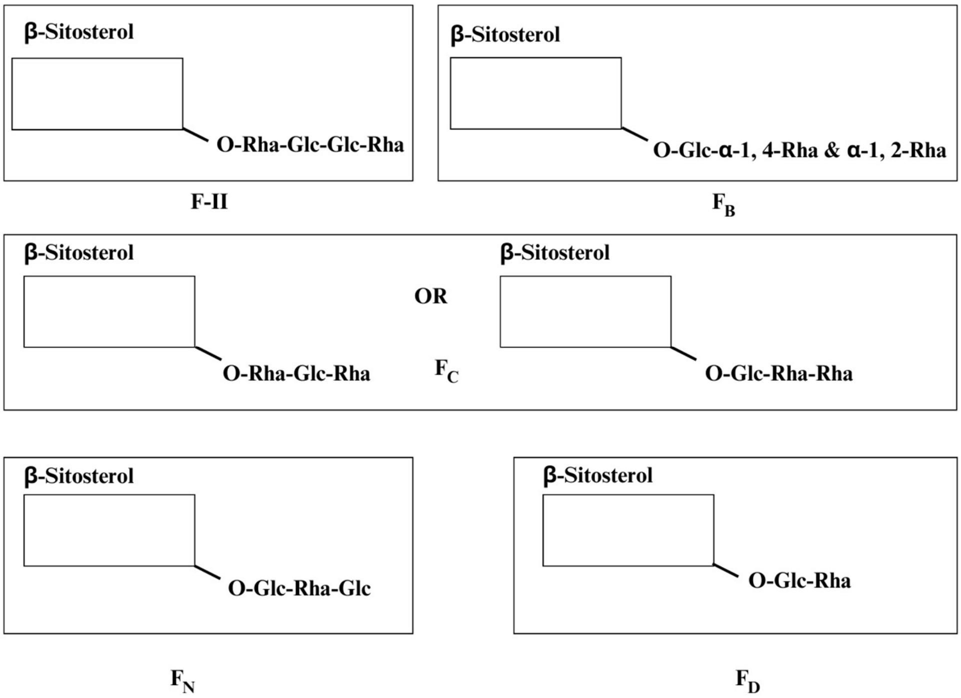

Figure 3. Structures of main flabelliferins present in palmyra palm.

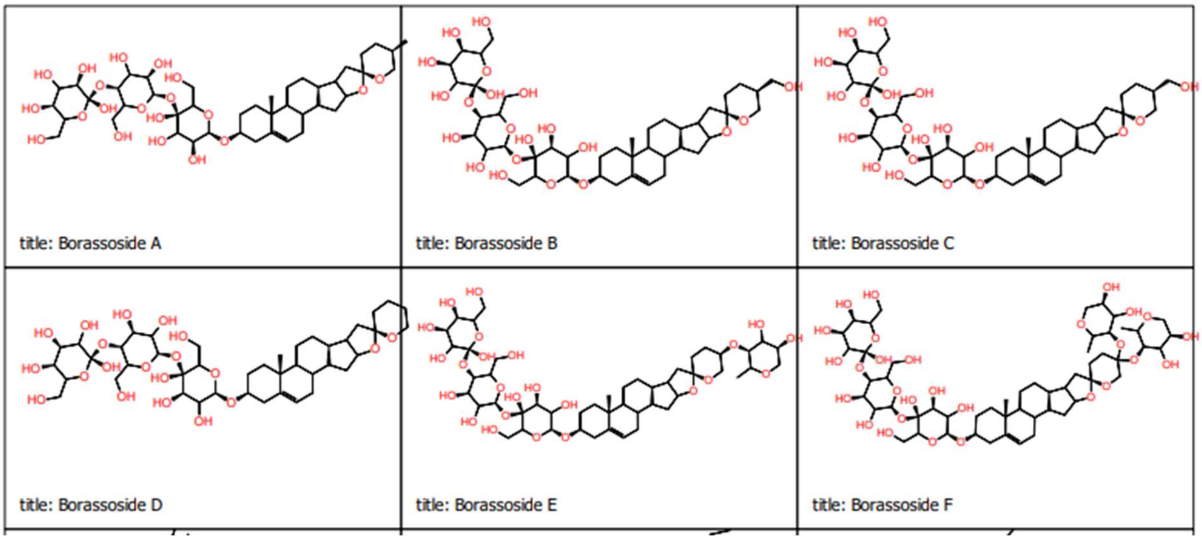

Figure 4. Structures of borassosides present in palmyra palm.

5. Biological activities of flabelliferins

Different types of flabelliferins extracted from the palmyra tree are found to have some significant biological activities. It is found that the hydrophobic molecules (carotenoids) in the palmyra fruit pulp increase the bioactivities of flabelliferins, especially in reducing the ATPase inhibition of F-II and enhancing the antimicrobial activity of F_B[23]. There are 14 types of flabelliferins that have been isolated so far[18]. A study conducted in mice has shown that the F-II flabelliferin extracted from the palmyra fruit pulp has anti-obesitic and anti-diabetic properties. Also, it is reported that F-II reduces blood glucose in a glucose challenge test by inhibiting glucose absorption in the intestinal lumen[24]. Also, F-II has the potential to inhibit the intestinal Na+/K+ pump and it can reduce hyperglycemia in the post-absorptive stage. This property is very helpful for type 2 diabetic patients[18]. The F_B flabelliferin is antimicrobial, and it can inhibit fungi, such as *Saccharomyces* *cerevisiae* and *Aspergillus oryzae*, and some other bacterial strains, including *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, *Escherichia coli*, *Bacillus licheniformis*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Proteus rettigeri*, and *Acenobacter calcoaceticus*[18]. **Table 1** sheds light on the different types of flabelliferins and their bioactivities. Flabelliferins from palmyra palm flour are found to be potential larvicides for the dengue mosquito *Aedes,* and the flabelliferin type is suspected to be the F_C flabelliferin[25].

Table 1. Different types of flabelliferins and their bioactivities.

Type	Description	Molecular formula	Bioactivity
F-I	Tetraglycoside	-	Not reported
F-II	Tetraglycoside	β Sitsosterol-O-Rha-Glc-Glc-Rha	Reduces intestinal glucose uptake and is anti-diabetic and anti-obesitic
F_B	Triglycoside	β Sitsosterol-O-Glc-α-1, 4-Rha and α-1, 2-Rha	Antimicrobial, inhibitor for SARS-CoV main proteinase, SARS-CoV main protease, and human cellular transmembrane serine proteinase
F_C	Triglycoside	β Sitsosterol-O-Rha-Glc-Rha or β Sitsosterol-O-Glc-Rha-Rha	Not reported
F_N	Triglycoside	β Sitsosterol-O-Glc-Rha-Glc	Not reported
F_D	Diglycoside	β Sitsosterol-O-Glc-Rha	Not reported
F_E	Diglycoside	-	Not reported
F_F	Monorhamnoside	-	Not reported
F_G	Monoglucoside	-	Not reported

*Another five flabelliferins have been extracted in very small amounts. However, no studies have been conducted on their structures and bioactivities yet.

A recent study has shown that flabelliferin B from *Borassus flabellifer* has the potential to inhibit SARS-CoV main proteinase and can act as an inhibitor for COVID-19 main protease. In this study's *in silico* analysis, six phytochemicals—namely, flabelliferin, marmelosin, piperine, ocimin, curcumin, and leucoanthocyanin—were analyzed. Three drug compounds, which were nelfinavir, remdesivir, and hydroxychloroquine, were used as the positive control drugs. The inhibition activity against one SARS-CoV-2 viral protease, COVID-19 main protease (SARS CoV-2, 3CLpro/Mpro), two coronavirus proteases, SARS-CoV main peptidase (SARS CoV Mpro), SARS-CoV main proteinase (SARS CoV 3CLpro), and one human cellular transmembrane serine protease (TMPRSS2) was studied. Flabelliferin showed the potential to inhibit SARS-CoV main proteinase much better than the positive control drugs and the other molecules. Also, flabelliferin was found to be the second-best inhibitor for COVID-19 main protease and a potential inhibitor of human cellular transmembrane serine proteinase among the other molecules tested in the study. The study additionally suggested that with further clinical studies, flabelliferin and the other molecules analyzed in the study can be used as therapeutics against COVID-19[26].

When it comes to the bioactivities of borassosides, only a few studies have been conducted. Out of the various medicinal activities of borassosides, as highlighted in **Figure 5**, a study has reported that they are antifungal, particularly borassoside E[20]. Borassoside E is found to show an oxidative burst suppressive activity[13]. **Table 2** sheds light on the different types of borassosides and their bioactivities.

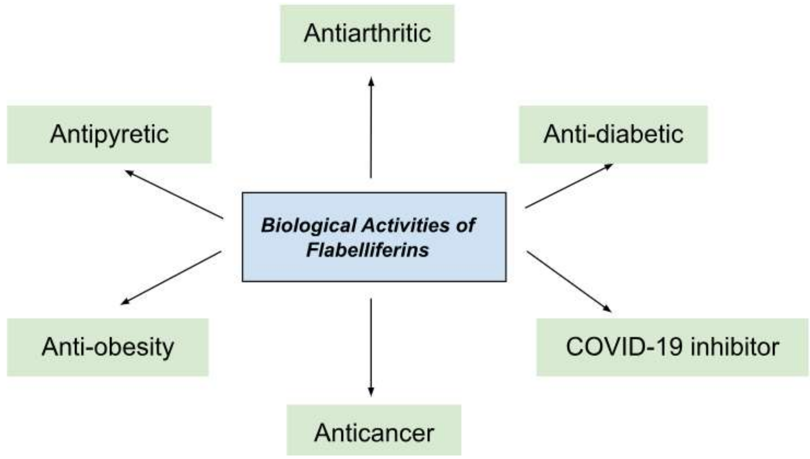

Figure 5. Various medicinal activities of flabelliferins.

Table 2. Different types of borassosides and their bioactivities.

Type	Molecular formula	Structure	Bioactivity
Borassoside A	$C_{45}H_{72}O_{16}$	yamogenin 3-O-α-L-rhamnopyranosyl(1→4)-α-L-rhamnopyranosyl(1→4)-β-D-glucopyranoside	Not reported
Borassoside B	$C_{45}H_{72}O_{18}$	23α,27-dihydroxydioscin	Not reported
Borassoside C	$C_{45}H_{72}O_{18}$	23α,27-dihydroxyyamogenin 3-O-α-L-rhamnopyranosyl-(1→4)-α-L-rhamnopyranosyl(1→2)-β-D-glucopyranoside	Not reported
Borassoside D	$C_{39}H_{62}O_{12}$	aglycone and diglycoside	Not reported
Borassoside E	$C_{45}H_{72}O_{16}$	dioscin and yamogenin 3-O-α-L-rhamnopyranosyl(1→4)-a-Lrhamnopyranosyl(1→2)-β-D-glucopyranoside	Oxidative burst suppressive Antifungal
Borassoside F	$C_{51}H_{82}O_{20}$	diosgenin 3-O-α-L-rhamnopyranosyl(1→4)-α-L-rhamnopyranosyl(1→4)-[α-L-rhamnopyranosyl(1→2)]-β-D-glucopyranoside, and yamogenin 3-O-α-L-rhamnopyranosyl(1→4)-α-Lrhamnopyranosyl(1→4)-[α-L-rhamnopyranosyl(1→2)]-β-D-glucopyranoside	Not reported

6. Scope and challenges

Palmyraculture paves the way for the plantation, utilization, and sustainable living based on the palmyra palm tree[4,27,28]. Understanding the chemical and biological aspects of two of its integral biomolecules, flabelliferins and borassosides, further extends the scope for exploration of the medicinal and nutritional values of different parts of the tree. Even though there have been a lot of research works done to find different flabelliferin and borassoside structures, the knowledge of their whole chemical composition is still insufficient. Out of the 14 types of flabelliferins identified, the structures of five flabelliferins have not yet been studied and the bioactivities of eight have not been tested yet. The bioactivities of only one borassoside have been explored so far. Thus, future researchers will have to focus more on these areas, which will help find more medicinal and nutritional values in palmyra palm. Moreover, this information, backed by pharmacological and physiological evaluations, will help identify their full nutraceutical potential.

When it comes to the pharmaceutical industry, thorough research of these biomolecules can go on to help with designing anti-inflammatory and anti-oxidant drugs. However, strict adherence to clinical test results and optimization are critical. From a nutraceutical perspective, *Borassus flabellifer* has the potential to be an in-demand health supplement. For this, their bioavailability and regulatory compliance need to be monitored.

Additionally, in the food industry, it has a major scope when used as a functional ingredient that assists in healthy nutrition requirements. Again, consumer preferences and regulatory requirements may pose challenges.

7. Conclusion

Palmyra palm is a naturally gifted medicinal plant, and a lot of studies have been conducted on the important biomolecules, including flabelliferin and borassosides, present in different parts of the tree. The exploration of these compounds here is highlighted by both their complexities and potentials. Different types of flabelliferins and borassosides have been extracted; some of their structures have been identified and some of the structures are not clearly established. While there have been efforts to understand their compound complexities, only surface-level discoveries have been made in this regard, and much more is yet to be uncovered. A limited number of studies have been done on the bioactivities of these molecules. Extensive research on flabelliferins and borassosides has the capacity to offer major scientific discoveries. Due to their distinct and structural uniqueness, their nutraceutical significance will be strengthened. For conducting further studies, it is important to determine the structure of all the flabelliferins and borassosides present in palmyra palm. Understanding the biomedical values of these molecules will lead to the development of therapeutics in the near future. This initiative will not only help unleash palmyra palm's full potential for medicine but also set the path for scientific curiosity. Through further research and innovative treatments, human health and quality of life will be profoundly impacted.

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Conflict of interest

The authors declare no conflict of interest.

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