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THE APPLICABILITY OF PALM TREES IN PHARMACEUTICALS AS EXCIPIENTS WITH A SPECIALEMPHASIS ON PALM SUGAR: A REVIEW.

***Saranga Shekhar Bordoloi, Tapash Chakraborty, Asha Das, Jakirul Islam, Damanbhalang Rynjah and Bitopan Baishya.**

Department of Pharmaceutics, Girijananda Chowdhury Institute of Pharmaceutical Science, Hatkhowapara, Azara, Guwahati-781017, Assam, India.

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***Corresponding Author**
Saranga Shekhar Bordoloi
Department of Pharmaceutics, Girijananda Chowdhury Institute of Pharmaceutical Science, Hatkhowapara, Azara, Guwahati-781017, Assam, India.

ABSTRACT

Palms like Sugar palm, palmyra palm tree, date tree, coconut palm, raphia palm, oil palm, sago palm & nypa palm fall under the family of Arecaceae, which are well known for their sweet sap from where we get sugar. Sugar from palm is generally used locally in desserts as a sweetener. Generally, this sugar is consisting of significant amount of fructose & glucose rather than only sucrose, but still, the major palm sugar content is sucrose. Sugar obtained from palm has also been seen to having less GI (Glycaemic index) value compare to cane sugar, so this sugar has great health benefits. Many Palm products including sugar, are used in pharmaceuticals as excipients. Palm has been seen to be used as binder, starch source, oil, bioethanol, gums, super-disintegrants, nanocrystalline cellulose, microcrystalline cellulose, masking agent, etc. As we found that sugar is highly soluble in water, it can be used to form a solid solution with BCS-II classification drugs to increase the bioavailability of the drug as we know aqueous solubility is directly proportional to bioavailability. So, we can also use Palm sugar for this purpose.

KEYWORDS: Palm, Palm sap, Palm sugar, Palm sugar content, Palm excipients.

INTRODUCTION

The excipients of natural sources have countless benefits compare to their synthetic equivalents as these are compatible, low cost, and easily obtained. Due to the elevating

realization for natural excipients, these are majorly polymers of natural source, the pharmaceutical manufacturing is getting more motivated towards the use at various formulation development. The plant-derived excipients of herbal origin are carrageenan, talin, fat from animals, styrax, agar-agar, Arabic gum, Shiraz gum, and various others which are used as natural pharmaceuticals excipients. It can be helpful for many types of formulation developments as being non-reactive and involving fewer regulatory requirements as estimated to their artificial counterparts.[1] Sugars as excipients have many claims, for example, they are used in compressed tablets and other dosage forms also. Mostly helpful as excipients as compressible sugar (sucrose), sugar esters, sugar laurate, crystalline malt sugar, a sugar alcohol (mannitol), and D-glucose. Initially, sugar-based excipients were applied for hiding the awful taste. Recently, they are found to help elevate compressibility or used for their hydrophilic/ hydrophobic properties and included in nanosuspension & particles as sugar esters.[2]

Sugar obtained from the palm is an ordinary sweetening agent obtained from sap/nectar composed from the florae of many classes of various types of palms like Arenga pinnata, Borassus flabellifer, Phoenix dactylifera L., Cocos nucifera, etc all belong to the family of Arecaceae. This sweetener has been utilized as a common and substitutes sweetener in the Southeast and South Asian counties, such as Indonesia, Philippines, Thailand, Malaysia, and India in such counties, the various types of palm trees are grown naturally in abundance. Countries like Indonesia and the Philippines are the main palm sugar manufacturers on the globe. Sugar from the palm is mostly utilized in soy sauce, drinks, sweets, and numerous items of traditional diets. Its usage is considerably enjoyed and acknowledged for the sense of taste, color & flavor progress of the delicacies. Sugar from the palm is primarily utilized in soy sauce, cuisines and beverages, candies, and numerous pieces of stuff of traditional foods. Its usage is very considerable and acknowledged for the good taste, color characteristics, and also flavor progress of the beverages and diets. The usage of sugar obtained from palm trees as soybean sauce sweetener extremely affects the soybean sauce taste due to the presence of extra 70 essential oils. The usage of sugar from palm also affects the textural characteristics, appearance, and flavor of cookies.[3] The palm syrup is obtained from naturally grown palm trees. Maximum of these molasses is generally consumed and usually produced as bottled juice as the bottled juice from the palm tree, palm wine, palm sweeteners. Since pure palm syrup is having a content of higher amounts invert sugar, it’s fairly tough to progress or convert into novel products which make the higher cost than the current products.[4] Cane

sugar is still the widely utilize sugar, but they cause a health problem. Sugar alcohols like mannitol have low calories but it's not quite economical to use. Palm and coconut sugars could be healthier in terms of GI value compared to cane sugar.[5]

Different types of sugar-producing Palms

Palmyra palm: Palmyra palm (Borassus flabellifer Linn.) belonging to the family of Arecaceae, grows naturally stretching from the Persian Gulf to the Cambodian-Vietnamese boundary and is generally cultivated in India, Southeast Asia, and Malaysia, and rarely in other warm regions, including Hawaii and southern Florida. Palms are trees that profit the environment naturally, as they re-establish damaged earth, demanding very slight water in this process.[6] When the sweet juice from the budding and various materials from leaves, trunk, and underground sprouts, a slim orangish flesh covering the fibers of the completely matured fruit is eaten fresh or it is dried as a paste. The sizeable seeds, when young, before the shell solidifies, include jelly-like kernels prized as edibles. Commonly palmyra palms are tapped to make fresh or fermented drinks, syrup, and sugars. They produce sugar yields that are higher than sugarcane production. The palmyra palm (Borassus flabellifer Linn.) is an influential sugar-generating tree that is broadly distributed in humid Asian countries.[7] It generates sugar yield better than cane sugar.[8]

Coconut Palm: The coconut palm (Cocos nucifera) legendarily known as the tree of life, belongs to the family Arecaceae and subfamily Coccoidea, which includes 27 genera and 600 species. Worldwide, the coconut palm can be found naturally occurring in the forests of many tropical and subtropical islands and coastal ecosystems in about 86 countries, frequently dominating the low-lying tropical atolls of the Pacific.[9] Phytochemical analysis of the coconut mesocarp ethanolic extract discovered that the existence of phenols, tannins, leucoanthocyanidins, flavonoids, triterpenes, steroids, and alkaloids while a butanol extract showed triterpenes, saponins, and condensed tannins Especially, flavonoids having antioxidant property are widely present throughout.[10] Coconut sugar is obtained from pure fresh coconut sap and consisting of 78–89 g/100 g sucrose the present research displayed that coconut bud sugar may have gluten, starch, sugars from coconut or palm oil. Coconut bud sugar absorbs moisture that agglutinates it. Clumped sugar causes difficulty to dose. Extra added starch absorbs moisture, to keep it dry, and prevents agglutination. By the addition of wheat starch, gluten is also made. This can cause a problem for gluten-sensitive people (e.g., as in celiac disease).[11]

Coconut juice is lighter in color having a low browning index, which is perfect for food handlers for sugar preparation.[7]

Sugar Palm: Sugar palm (Arenga pinnata) belonging to the family Arecaceae is a versatile type of palm from which is signified as edibles, drinks, lumber, polymers, and bio-composites, etc. Lately, it is also started to contribute as a source for renewable energy as bio-ethanol made from sugar palm juice. Other products are also produced from sugar palm, there are sugar and fibers.[12] The immature plant roots have been seen treating stones in kidneys and odontalgia in countries like Malaysia. In Asia's Southeast region, its sugar is valued as a local and homeopathic treatment and also for refreshment. The Philippines uses stems and leafstalks of the plant as diuretic and anthelminthic. Sugary sap is obtained from both sex of flowers, the peduncle is bruised by beating over several days, and then an incision is done in the peduncle for the sap to flow out which is then collected in a vessel the fresh sap is collected from the vessel two times in 24 hours in a hygienic container. The bulk of sap in male palm flower is high and easier to extract. Sugary sap from the cut inflorescence makes a fresh drink called saguir, nira, or lahang. On standing for several days, it becomes fermented and provides toddy, arrack, or tuak containing about 30% alcohol. On fermentation for several weeks, it is converted to vinegar (acetic acid) and also with further distillation into wine. The juice can be boiled down to make arenga syrup or allow to set in molds to form arenga sugar, called Gur in India. Arenga sugar is dark brown and contains many impurities which cause it to have a short shelf life. It has a distinctive characteristic taste. Syrup or sugar from arenga is utilized in every dish, candies, and drink. It's a perfect sweetener and flavor enhancer for many desserts. To obtain vinegar, the sap is put in vitrified earthen jars for 3–4 weeks (T. K. & Lim, 2012a).

Date Palm: *Phoenix dactylifera L*. is said to be the oldest and chief principle and primeval tree in Southwest Asia and Northern Africa. It is also grown in Australia, Mexico, South America, southern Africa, and the US. The date palm has its place in the Aceraceae family.[13] All date varieties tested exhibited high concentrations of phenolic and flavonoid components as well as high antioxidant activities.[14] Dates have fewer fats and proteins but rich in sugars like fructose and glucose. It is a high source of calories.[15] The most important components of dates are carbohydrates in particular sugars, which can constitute up to 78% and provide a readily available source of energy to the human body. t the total carbohydrate contents of three dried Omani date varieties (Khasab, Khalas, and Fardh) ranged between 68.53 and 75.37 g/100

g of date flesh. The highest value 75.37 g/100 g was observed in the Khalas variety. The glucose, fructose, and sucrose contents ranged from 29.04 to 34.53 g/100 g, 20.72 to 23.65 g/100 g, and 1.86 to 2.34 g/100 g, respectively. The highest glucose level was found in Khasab whereas the highest fructose was observed in Khalas. The region of production and variety can significantly affect the glucose and total sugar contents of date fruit Glucose and fructose contained in date flesh are readily absorbed during the digestion and can lead to a rapid elevation of blood sugar.[16] Dates shows reduce in cholesterol and an increase in HDL. It has also been seen that date consumption does not result in increased triglyceride and LDL levels, or BMI.[17]

Raphia Palm: Raphia palm (*Raphia hookeri*) has a disjunct distribution between Africa and the Neotropics. In Africa, it is widely distributed, occurring from the west through to eastern and southern Africa, and has one species in Madagascar (*Raphia farinifera*). *Raphia taedigera* is native in South and Central America.[18] It's used furniture, construction, food, clothing & edible oil. The Raphia palm has the largest leave amongst the other palms in Africa. It produces a sap which is drunk by millions of people in Africa.[19] Raffia palm fibers are potential reinforcement materials for making cost-effective polymer-based composite.[20] The fruits possess Alkaloids, Saponins, Flavonoids, Glycosides, and Tannin's concentration are present.[21] The raffia palm sap syrups (like honey) also contained Milliard reaction products and phenolic compounds, alkaloids, saponins, and glycosides, and exhibited broad-spectrum antimicrobial activity.[22]

Oil Palm: The oil palm (*Elaeis guineensis* Jacq.) has been reported to originate along the Gulf of Guinea in West Africa. The various parts of the tree have been used locally and traditionally for various medicinal purposes. Some of these uses have been proved by scientific experiments. Palm oil is extracted from the mesocarp of the fruit and is used traditionally for the treatment of headaches, pains, rheumatism, cardiovascular diseases, arterial thrombosis, and atherosclerosis due to its rich phytonutrients.[23] It has high polyphenols and contains constituents like epigallocatechin, catechin, epicatechin, epigallocatechin gallate, epicatechin gallate.[24] The fruits shown containing phenols, vitamin E, protein and carotene decreased as harvesting time increased. In contrast, enzyme activity in lipase increased as harvesting time increased. The highest lipase activity was achieved at 120 h of harvesting and the activity increased to 4.76 U/mg after partial purification. Therefore, palm lipase was used as the catalyst for biodiesel production using waste cooking oil as substrate.[25] Glucose was found to be the

dominant sugar in all parts, accounting for approximately 86.9%, 86.3%, and 65.2% of the total free sugars contained in the inner, middle, and outer parts, respectively. In addition to glucose, significant amounts of sucrose and fructose were contained in the sap.[26]

Sago Palm: The sago palm (*Metroxylon sagu* Rottb.) is one of the underutilized food crops that has the promising potential to strengthen food security programs especially in Sarawak, Malaysia. Thriving well in harsh environments such as the freshwater swampy area, the sago palm is also unique for its ability to store starch within its trunk, compared to other types of starch storage organs. With its superb high starch yield as compared to commonly found starch sources such as corn, rice, and wheat, it is deemed as the palm of many uses.[27] Results from this study indicated that starch, amylose, fat, protein, and ash content of the starches accumulated plentifully at the base of the palm then lessen towards the middle height for all growth stages except for Bubul stages. The highest starch content was found at the Plawei stage (94.2%) and Angau Muda stage (97.9%) at the base and middle height, respectively. Granule size distributions were similar as the palm grows to the xiv later growth stages. The highest mean diameter of sago starches granules was found at the Angau Muda stage (33.3μm) at base height. Angau Muda stage has the highest resistance where syneresis does not happen after five cycles of freeze-thaw analysis. The physicochemical properties characteristics of sago starch from both different growth and height did not differ significantly.[28] An inflorescence stalk of the sago palm may be beaten with a wooden mallet each day for 2–3 weeks to loosen the sap and it exudes. Sugar can be produced from sago by boiling the sweet unfermented sap. Generally, the sap is thickened into a desirable consistency by boiling it in an open kettle.[29]

Nypa Palm: *Nypa fruticans* are classified as palm. It is a native plant of Asia. According to reports native distribution and habitat of nypa are the South and Southeast Asia, in tropical rain forests at brackish water swamps of tidal rivers. Nypa thrives in mangrove areas in Jambi Province but is underutilized. Several parts of nypa tree have been utilized such as leaves for thatching or roofing and nypa sap for making sugar.[30] The chemical compounds of granulated nipa palm sugar made from the sap of nipa palms had water, protein, fat, reducing sugar, sucrose, phosphorus, and potassium content.[31] Studies conclude that vinegar produced from nypa palm can modulate either the innate immune response (phagocytic activity) and adaptive immune response (cellular and humoral immunity), and the nypa palm vinegar benefits human health can be investigated as well.[32] Unripe endosperm extract of *Nypa fruticans* showed high total phenolics, total flavonoid content, and antioxidant capacities

as compared to ripe endosperm extract. Chlorogenic acid, protocatechuic acid, and kaempferol were identified as major compounds in the extract. Thus, unripe endosperm extract of the plant could be used as a natural antioxidant.[33]

Various Excipients Obtained from Palm

Binders: Within the scope of this work, date syrup showed excellent properties as a tablet binder in comparison to starch paste or sucrose syrup for the granulation of both water-soluble and water-insoluble materials. Also, better flavouring and masking taste have been noticed from an evaluation by human volunteers demonstrating the usefulness of the date syrup as a sweetener and flavouring the tablets in addition to its use as a binder. shows the specific gravity and the viscosity of the binders' solutions tested. It indicates the similarity between the diluted date syrup, the diluted sucrose syrup, and starch paste in their specific gravity. However, starch paste showed a noticeably higher viscosity than dates syrup or sucrose syrup (more than 12 times of their values). The rheological properties of the date syrups seem to be either pseudoplastic or plastic due to the high negative value of the intercept (-19) which indicates the presence of the yield value of 32.33. This is could be explained by the presence of date particles in a suspension (plastic) and/or the presence of natural date solution (pseudoplastic).[34] Dried date palm fruit is a natural product that is non-toxic, biodegradable, and biocompatible that can be employed as a pharmaceutical binding agent for immediate release dosage forms. The granules manufactured with date palm had good flow properties and satisfactory compressibility which led to tablets with less variation in uniformity. The tablets had good uniformity of weight, thickness, and diameter, hard and less friable than acacia and tragacanth as its concentration increases; and a better binder than tragacanth.[35]

Super disintegrant: Date trees contain crucial substances that can give easily as pure date palm cellulose and so instead of burning the dead trees their cellulose which can used conventionally in pharmaceutical industry. Brine seawater contains essential divalent cations which produces water-insoluble silicate salts of calcium and magnesium upon reacting with sodium silicate) which is an inexpensive product of sand silica and soda). Thus, it is possible to produce mineral-fibre solid dispersion through the inclusion of water-insoluble silicate salts within the date palm cellulose and so improving date palm cellulose compaction and disintegration properties. The tablets produced using water-insoluble calcium with magnesium silicate salts and date cellulose were tougher and had lesser disintegration time at all

compression forces compared to those made with date palm cellulose. The produced excipient had excellent compaction and disintegration properties and could be used as a super disintegrant and tablet binder in pharmaceutical industries.[36]

Bioethanol: Ethanol is a chemical compound which has many utilizations, like beverages well as in chemicals, pharmaceuticals, and biofuels.[37] Bioethanol is used as solvent in the laboratory, pharmaceutical, cosmetic, medical and biomedical field. It is made by the help of biological substances like plant parts, algae or biomass to make the solvent.[38] Bioethanol isa raw material for many products like chemicals, solvents, pharmaceuticals, cosmetics, medicines, and beverages. The palm "*Arenga pinnata*" is a versatile tree grown in Malaysia. Besides producing sugar, it is used for products like ropes, filters, sweepers, and rooftop materials. Nowadays, researchers finding new ways to produce ethanol, which can obtain from its sugar.[39]

Nanocrystal cellulose: Owing to the fascinating behavior of nanocrystal cellulose like biocompatibility, non-toxicity, hydrophilic nature as well as self-assembly in the liquid state, it has been extensively employed as an emulsifier, thickener, cosmetics, and pharmaceutical applications.[40] Nanocrystal cellulose derived from sugar palm (*Arenga pinnata*) bunches are qualified in all the criteria, to be used as binders & fillers in the tablets.[41]

Microcrystalline cellulose: MCC is a famous excipient which is mostly utilize in pharmaceutical formulations. It has application for binder, disintegrant, absorbent, diluent, lubricant & anti-adherent. Its high utilization for microcrystalline cellulose in pharmaceutical formulations have led in the search for organic materials to produce microcrystalline cellulose.[42] Oil palm (*Elaeis guineensis*) biomass and leaves can be applicable for a good source of MCC.[43]

Gums: In the past we have seen the positive roles of herbal gums as pharmaceutical ingredients. Gums became important excipients in many pharmaceuticals' preparations due to their richness, biodegradability, compatibility, and low cost. They have prominent usage in pharmaceuticals as binding excipient, disintegrating excipient, suspending agents & emulsifying agent. Gums nowadays used as matrix-forming ingredient in new type of drug delivery methods.[44] Several carbohydrates like, gelatine, glucosamine sulphate, guaran, xanthan and deacetylated chitin are being studied as carriers for specific drug delivery in colon.[45] The mineral element compositions are within the range specified by WHO are

present in the Raphia gum obtained from Raphia Palm (*Raphia hookeri)*. Raphia gum was also found to be pH sensitive and may therefore be useful in intestinal/colon drug delivery.[46]

Oils: Most frequently chosen excipients for preparing oral lipid-based formulations were dietary oils composed of medium- (e.g., coconut or palm seed oil) or long-chain triglycerides (e.g., corn, olive, peanut, rapeseed, sesame, including hydrogenated soybean or vegetal oils).[47]

Palm tree oil is natural-based product which contains fatty acids is used in lipid-based drug delivery. It has long-chain and medium-chain triglycerides, individually, having phytonutrients like tocotrienol, tocopherol and carotenes. All these compounds can used in lipid-based preparation can show hydrophobicity, lipophilicity, lower aqueous solubility drugs. Application of these oil for drug delivery design seemed to progress the aqueous solubility of drugs, controlled emulsification for the product for its emulsifier & its surfactant, to elevate drug permeability and presentation, and increase in shelf-life of drug.[48]

Masking Agent: Taste is a significant criterion in managing oral drugs and is a serious aspect to be measured while formulating drugs for oral routes, which dissolve in mouth, oral tablet and other formulations which comes in contact with taste buds. Good flavour and feel are found to meaningfully affect marketing of products. Objectionable sense of taste is one of the serious formulation difficulties met by, maximum of drugs.[49] Sucrose is having the best taste masking abilities no influence in the wanted instant release profile. The masking could be further improved by using Witocan H, which is a triglyceride based on coconut/palm (*Cocos nucifera*) kernel oil instead, but the addition of the Benecoat BMI-40 bitterness suppressant is needed.[50]

Starch: Starch is one of excipient used in manufacturing of tablets. Chemically, starches are polysaccharides, composed of various monosaccharides or sugar (glucose) molecules linked together with α-d-(1-4) and/or α-d-(1-6) linkages. Starch is examined as a good excipient in new drug delivery classifications for nasal delivery, oral delivery, periodontal delivery, and other site-specific carrier systems. Based on applications, particular starches are accessible as a disintegrants, diluents or binders.[51] Sago starch is an unofficial starch obtained from the sago palms (*Metroxylon sagu Rottb*.), the physicochemical properties and its potential for use as a body powder and lubricant in certain surgical and diagnostic materials has been studied & investigated.[52]

CONCLUSION

The papers reviewed provide ideas on how Palm and its product is used as novel pharmaceutical excipients. Grounded on the studies, palms are an admirable basis of sugar which is obtained from their sap fluid. Palm sugar is mainly consisting of non-reducing sugar (sucrose) and having reducing sugar (glucose & fructose). As we reviewed that sugar has an extensive variety of utilization in pharmaceutical excipients, it is applicable in tablets, powders and it's also had functions like taste masking, for many oral dosage procedures. It is also comprised in nano-suspensions and nanoparticles as sucrose esters. The drugs which are less bioavailable due to poorly aqueous soluble drugs can be increased by the solid dispersion with the drug-using sugars as carriers.[53] Sugars have an excellent aqueous solubility which will help to elevate the water dissolving property of the drug, as we know bioavailability directly related to the aqueous dissolution of drug. Many palm types have been specified to pay to the ground of pharmacy, the species like Palmyra Palm, which is known species of palm & found in abundance in the whole Southeast-Asia region. So, there are no evidence researches have made regarding the utilization of its sugar or any other part of the plant, as an excipient in the research of pharmaceuticals. Unlike date tree sugar syrup which has shown to be good tablet binder, so sugar gained from the further palm species should also be evaluated for their usage as an excipient.

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