Therapeutic effects of bioactive compounds of dates fruit (phoenix dactylifera) produced by fermentation process: A Review

Duaa Khalid Khlaif

Education Directory of Al Muthanna, Samawa – Al Muthanna Province.

duaa2020bio@gmail.com

Received 11 Apr. 2025, Accepted 23 June. 2025, published 30 Dec. 2025.

DOI: 10.52113/2/12.02.2025/21-34

Abstract: This study attempts to describe scientific investigations on date palm fruit and human health. Dates are a significant source of numerous nutrients carbohydrate content and abundance of vital minerals and vitamins. It is also abundant in phenolic acids, tannins, carotenoids and flavonoids, all of which have medicinal benefits for a variety of illnesses. By using fermentation to release these chemicals and then examine their medicinal and therapeutic qualities, the outcomes demonstrated that the most crucial of these treatments are antimicrobials, antioxidants, gastrointestinal protective, antidiabetic, and anticancer. The fermentation process can be used to benefit from the by-products of dates in the creation of new products. The potent and advantageous components of *Phoenix dactylifera*, including as flavonoids, phenolics, amino acids, and fatty acids, may be responsible for its pharmacological benefits, and minerals. The goal of this review was to describe *Phoenix dactylifera 's* pharmacological preventative and therapeutic potentials.

Keywords: date palm, bioactive compounds, fermentation

1. Introduction

Phoenix dactylifera grows in dry areas of many of desert nations including Iraq, north Africa, Iran, the United Arab Emirates and Saudi Arabia. *Phoenix dactylifera* is a member in the genus Phoenix and family Arecaceae. Dates are eaten as fruit or processed into flesh and sap to make sauces and other foods also used as natural dietary sweets, as prepared food, and as a dietary supplement for all consumer groups, particularly for people who have trouble swallowing. Dates are rich in carbohydrates, mostly fructose and glucose, as well as a variety of vitamins and minerals. Specifically, the sugars found in dates are potentially good sources of carbon that can be fermented by microbes [1,2].

In addition to its nutritional value and Due to its abundance in alkaloids, protein, fatty acids (lauric, linoleic, stearic, and palmitic acid), carotenoids, polyphenolic compounds, vitamins, tannins and flavonoids as well as various minerals like calcium, potassium, phosphorus and magnesium, it is used as a medical treatment for many diseases. So they have a larger impact on human health

since they include a variety of phytochemicals [3]. There are many studies and scientific research conducted on dates to extract its effective compounds for use in therapeutic and industrial purposes, such as the use of alcoholic and water solvents of different concentrations. Although there are many methods and solvents that were used to extract these effective compounds, one of the best ways to obtain these primary and secondary chemical compounds is through the use of bioprocessing technologies, which typically involve the application of microorganisms as whole cells through different application and under specific condition. A promising Fermentation is a procedure used to create unique items with altered physicochemical and sensory qualities, including flavor and nutritional components. Fermentation is an energy-efficient, moderately effective method of preserving food that lengthens its shelf life and removes the necessity for food preservation techniques. As a result, it is a technique that is ideal for usage in underdeveloped nations and remote regions without easy access to complex machinery. When beneficial microorganisms are utilized in fermentation, value-added products with significant commercial value are produced [4].

Any fruit that has sugar will naturally ferment; it just needs a warm environment and air that is home to yeast or bacteria to turn the sugar into carbon dioxide, glycerol, and alcohol. However, the industrial fermentation process is carried out by picking the right circumstances and nutrient quantities for the necessary microbe to finish the process. Bacteria and molds have been used in fermentation process to produce compounds Antibiotics, riboflavin, monosodium glutamate, lactic acid, acetone, butyl alcohol, acetic acid, citric acid, and gluconic acid [5]. The goal of this review was to describe fermented *Phoenix dactylifera* 's pharmacological preventative and therapeutic potentials.

Taxonomic classification
Kingdom: Plantae
Division: Tracheophyta
Class: Magnoliopsida
Family: Arecaceae
Genus: Phoenix
Species: *Phoenix dactylifera* [6].

2. Phoenix dactylifera

Phoenix dactylifera has many health aids since it possesses a variety of secondary metabolites. It has a variety of pharmacological effects, comprising those that are effects that include antitumor, Hepato and reno-protective, immunomodulatory, neurological, cardiovascular, hypolipidemic, gastrointestinal, anti-inflammatory, antimicrobial, antiparasitic, antioxidant, and anti-toxin and wound healing [6]. The Phoenix dactylifera plant's fruits are used as an astringent and deterrent for intestinal issues.,

as a remedy for sore throats, colds, and bronchial catarrh, as well as to treat fever, edema, gonorrhea, and cystisis, liver and gastrointestinal problems, as well as to treat alcohol intoxication. Date saps, both fresh and fermented, were particularly high in iron and vitamin B complex, respectively. Hemoglobin-deficient anemic individuals can be treated with balanced dosage of fresh and fermented date sap alone, which will also raise vitamin B12 levels. [7]. Byproducts from dates can be utilized as raw materials to produce value-added products including bread yeast, probiotic fermented dairy products with dates, organic acids, exopolysaccharides, and antibiotics, among other goods [3].

3. Biochemical profile and nutrient content

Dates are very sugary and abundant in carbohydrates depending on the cultivar, step of ripening, and overall moisture content, comprise 50–88% of their weight in carbs. Water makes up the remaining one-fifth of the overall fleshy composition, while dietary fiber makes up the small amount of residual flesh. Dates are also rich in minerals, vitamins (particularly vitamin B), crude fiber, protein, lipids, and tannins [8]. Due to their abundance in bioactive chemicals and fermentable sugars, Date fruits and their byproducts provide a variety of starting points for microbial fermentation. Despite the fact that dates are now sold as fruits and processed goods, a sizable There are a number of missing dates every year. Conversely, though, effective microbial transformations may present an opportunity to meet consumer demand for wholesome and environmentally friendly foods while minimizing food loss [9].

3.1. Carbohydrates

Traces of polysaccharides, non-reducing carbohydrates like sucrose, and the reducing sugars fructose and glucose like cellulose and starches xylose, arabinose, and galactose—which normally comprise two-thirds of the date's total flesh—are the primary carbohydrates found in dates [8]. Because of the indirect relationship between dates' moisture level and sugar content, dates with a high moisture content are invariably lower in sugar. The sugar concentration of dates is the most crucial commercial feature, as it affects fruit processing as well as fresh consumption. Dates may be a source of refined sugar because of their comparatively high sugar content. The human body may use dates as an important energy source. The energy levels (kcal/100 g) were assessed for tested date fruit varietals. The findings demonstrated that Khodari, which was grown in the El-Qaseem region, had energy levels that were significantly greater ($P < .05$) than those of other types, followed by Suqaey and Anbarah [10].

3.2. Protein and amino acids

Dates contain very little levels of protein, their concentrations are higher than those of other fruits and rich in both essential (such as leucine and lysine) and non-essential amino acids (such as glutamic acid, glycine, and aspartic acid)., with amounts ranging from 1.7 to 4.7%. Shalaby, a Saudi variety, had a maximum protein level of 4.7%, while Mabroom, another Saudi variety, had a lowest protein content of 1.7%. Date varieties including Qush Balquan, Khalas, Barhi, Lulu, Deglet-Noor, and Medjool have median crude protein contents between 1.6 and 3.64. The fruiting stage of the dates can also affect the protein level; fresh dates had protein contents between 1.1 and 2.0%, whereas dried dates had protein contents between 1.5 and 3.0% [11]. Glutamic acid (16.44 g/100 g), phenylalanine (5.93 g/100 g), and leucine (6.10 g/100 g) are the three main amino acids found in date seeds. In contrast, another study found that after using an automatic amino acid analyzer, leucine (1.7 g/100 g), lysine (1.1 g/100 g), and phenylalanine (1.08 g/100 g) were the major essential amino acids and aspartic acid (1.72 g/100 g), alanine (1.2 g/100 g), and tyrosine (1.2 g/100 g) were the major non-essential amino acids figure 1 show the structure of these amino acids [12].

The building blocks of proteins, amino acids are essential for the synthesis of hormones and help specialized proteins called enzymes transform precursor molecules into active hormones [13]. hormones related to sexual activity, including estrogen and testosterone. Furthermore, studies have shown that certain amino acids, such as arginine, might improve sperm function and quality by lowering oxidative stress and heat without having negative consequences [14].

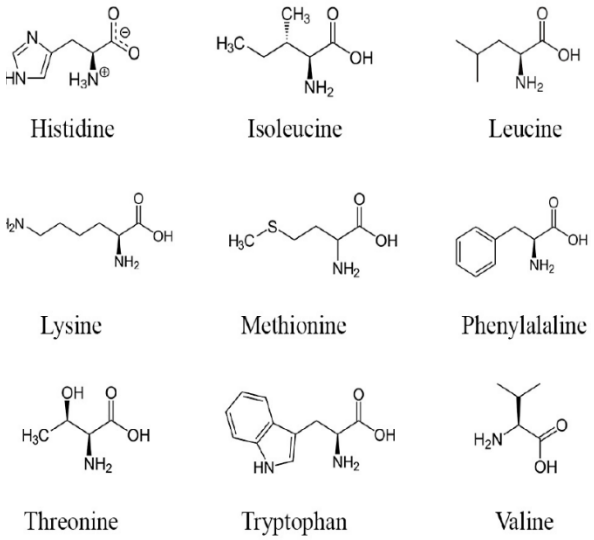

Fig (1): Structure of the main essential amino acids found in Date palm (14).

3.3. Oils and fatty acids content

Each variety has a different amount of oil in the date seed. Additionally, Two Tunisian cultivars showed greater levels (10.19–12.67%) in another investigation. The varietal effect of cultural conditions, extraction solvent type, temperature, and equipment. The fatty acid composition of all samples showed that they were primarily composed of SFA (saturated fatty acid) (47.88–54.13%) and MUFA (monounsaturated fatty acids) (38.38–44.43%) rather than PUFA (polyunsaturated fatty acids) (6.34–8.27%) due to the high

content of saturated fatty acids like lauric (21.72–44.38%), palmitic (9,65–11.38%), and monounsaturated fatty acids like oleic (38.67–44.38%). This increases antioxidant activity and implies high oxidative stability when combined with antioxidants like tocopherols. As a result, it is said to offer cardiovascular disease prevention. Furthermore, lauric acid's resistance to oxidation, capacity to create stable emulsions, anti-obesity benefits, control over energy metabolism [15]. The structure and operation of cell membranes depend on fatty acids. Essential fatty acids omega-3 and omega-6 are involved in physiological processes that could have an effect on reproduction. Prostaglandins, which are involved in essential activities including ovulation and implantation, are among the hormones that are synthesized and regulated by specific fatty acid types Figure (2) show structure of fatty acids [14].

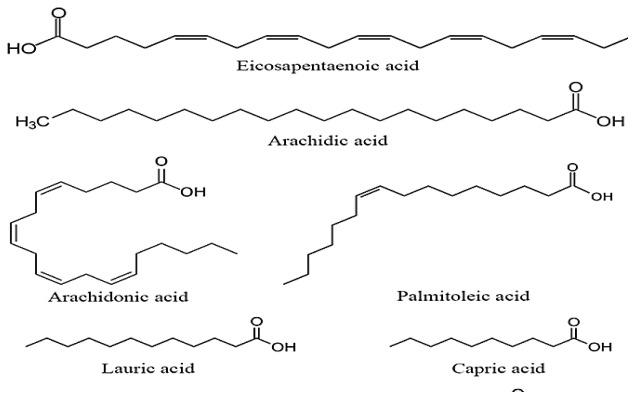

Fig (2): Fatty acids structure (14).

4. Bioactive compounds

4.1. Phenolic compounds

The structure of phenolic compounds, which are classified as one of the main aromatic secondary metabolites of plants. Phenolic compounds have a hydroxyl function on the aromatic benzene ring and one or more carboxylic acid groups figure 3. The two main categories of phenolic acids are derivatives of benzoic acid, which has seven carbon atoms, and derivatives of cinnamic acid, which has nine carbon atoms. Because they scavenge or capture free radicals, they are regarded as an effective antioxidant as show in figure (4), [16]. According to multiple study groups, dates are rich in phenolic acids, such as p-hydroxybenzoic acid, protocatechuic acid, vanillic acid, gallic acid, and syringic acid. fortunately, o-coumaric acid, p-coumaric acid, caffeic acid, and ferulic acid are among the several cinnamic acid derivatives found in dates. A different investigation discovered the primary phenolic acids, including sinapic acid, ferulic acid, and p-coumaric acid figure 3 show in seven different date fruit kinds grown in Algeria [17].

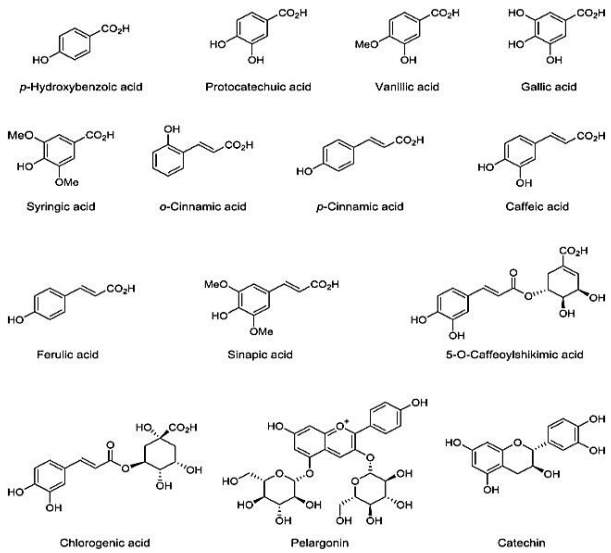

Fig (3): phenolic compounds structure (17).

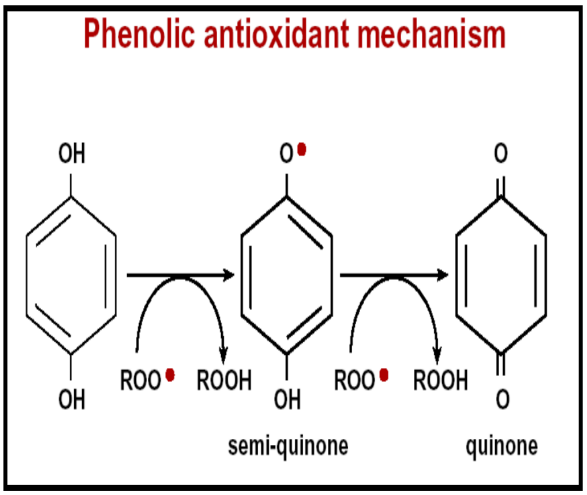

Fig.4: Phenolic antioxidant mechanism.

4.2. Flavonoids

A heterocyclic pyrane ring C chemically bonds two aromatic benzene rings A and C in the 15-carbon skeleton of flavonoids, a large class of secondary metabolites derived from polyphenolic plants. There are many different replacement patterns that are commonly used to replace this skeleton. Among the subclasses of flavonoids are flavones, flavonols, flavanones, flavanonol, isoflavonone, flavan-3-ols, and anthocyanidins. Flavonoids, which are found in many fruits and vegetables, have been demonstrated to offer important health benefits as antioxidants and anti-inflammatory agents. In Oman, the total flavonoid content of three significant date varieties—Khasab, Khalas, and Fardh—has been investigated at two edible maturity stages: Tamr and Rutab. In another study, 11 different Saudi date fruit varieties were discovered to contain apigenin, luteolin, quercetin, isoquercetrin, and rutin were found in 11 distinct Saudi date fruit cultivars in a different study. Amari and Hallawi date fruits were found to contain derivatives of kaempferol, a naturally occurring flavonol. Amari had a significant amount of five flavonols, while Hallawi had one major flavonol figure represent Bioactive constituents of date fruits [17].

.

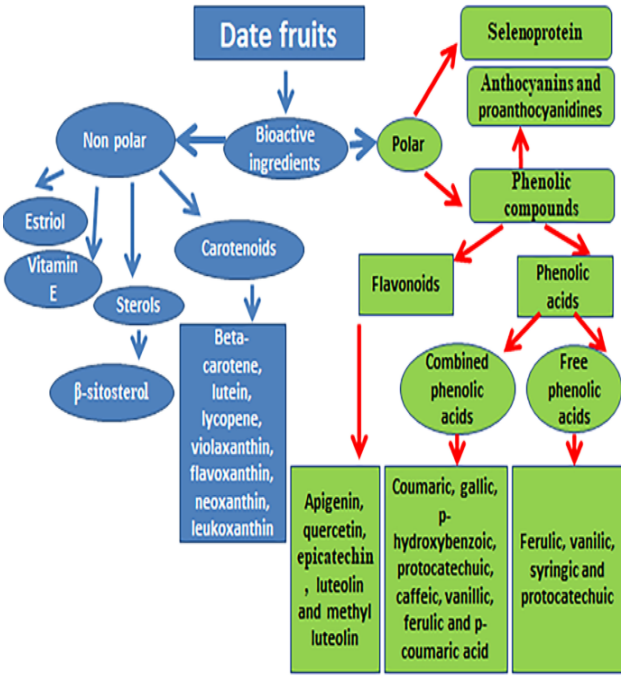

Fig (5): Bioactive constituents of date palm fruits (18).

5. Fermentation process:

The transformation of a sugar into an organic acid or an alcohol is the most widely used definition of fermentation. Many foods naturally ferment, and since ancient times, people have purposefully used fermentation to enhance the food's organoleptic qualities and preservation. The intentional industrial use of microorganisms like bacteria, yeast, and fungi in order to produce human-beneficial products

like biomass, enzymes, primary and secondary metabolites, recombinant products, and products of biotransformation is also referred to as "fermentation," though this term is also used more widely. [19].

5.1. Microorganisms used in fermentation:

Aspergillus, Fusarium, Penicillium, Rhizopus, and Trichoderma are among the filamentous fungi used in solid-state fermentation. Additionally, yeasts (Saccharomyces cerevisiae, Saccharomyces boulardii, and Candida sp.) and actinobacteria (Streptomyces thermonitrificans, Streptomyces chattanoogensis) are used in solid-state fermentation. Bacteria, particularly Bacillus megaterium and Bacillus mycoides, as well as Lactobacillus species including Lactobacillus acidophilus, Lactobacillus bulgaricus, Lactobacillus plantarum, Lactobacillus rhamnosus, Lactobacillus delbrueckii, and Lactobacillus coryniformis, are equally utilized in solid-state fermentation. Filamentous fungi and yeasts are perfect for solid-state fermentation because they can break down solid organic substrates in a low-moisture environment. It's interesting to note that solid-state fermentation uses Streptomyces spp., which are Gram-positive mycelial bacteria, due to their capacity to produce a variety of degradative enzymes, efficiently colonize solid organic materials, and tolerate harsh environmental conditions [20].

5.2 Limitations and Challenges

Although SSF offers numerous benefits over liquid cultivation, its primary disadvantages are its limited capacity to remotely monitor critical cultivation parameters like temperature, pH, dissolved oxygen, nutrient concentrations, or water content, as well as its inability to precisely control the microbial environment because of inadequate heat and mass transfers within the substrate. One of the main obstacles to process scale-up is the heat produced by microbial metabolism [21].

6. Applications and features of pharmaceuticals

Nutraceuticals in date palm have been shown to have a variety of health-promoting benefits. The many bioactive components found in the date palm's fruits, seeds, leaves, and other parts were credited with these health advantages [22].

6.1. Biochemical and Hematological parameters

Date palm is a good source of primary and secondary metabolites, including sugars, amino acids, phenolic acids, flavonoids, proanthocyanidins, carotenoids, phytosterols, terpenes, and sphingolipids, in addition to vitamins and minerals. It possesses a wide range of pharmacologic activities, such as immunomodulatory, antioxidant, anti-inflammatory, hepatoprotective, nephroprotective, anti-mutagenic, and anti-

cancer qualities, in addition to its positive effects on male and female fertility [23].

Figure (5) illustration biochemical and hematological parameters. To fully comprehend its therapeutic consequences, particularly with regard to women's health, more research is still needed. Furthermore, more research is required to fully understand the biological activities and unidentified phytochemical components of other Phoenix species [23]. *Phoenix dactylifera* fruit extract has protective effects against renal toxicity and oxidative stress via antioxidant activity, it was able to lessen the structural harm that cadmium caused to an adult's kidney tissue Wistar rat [24]. *Phoenix dactylifera* 's aqueous fruit extracts may have the ability to boost the liver's enhanced production of erythropoietin, which would then encourage the bone marrow to create more cells (haemopoiesis) and result in the effects on peripheral blood parameters shown in Wistar rats [25]. the impact of date pulp extract and palm sap (Phoenix dactylifera L.) on the transit activity of the digestive system in rats in good condition. This could support the long-standing practice of using palm sap and date pulp to treat digestive system problems including constipation [26]. The physicochemical characteristics of the bio-yogurt were enhanced by date juice, which also improved the probiotic bacteria's survival rate, which encouraged the development of healthy colon microorganisms. Animals fed diets treated with date juice from bio-yogurt generally had better feed intake, serum biochemical indicators, body weight, and hematological parameters. Additionally, the groups given bio-yogurt, which included date juice, frequently showed stronger immunological and haematological markers than other groups as well as lower total cholesterol and triglyceride levels [27].

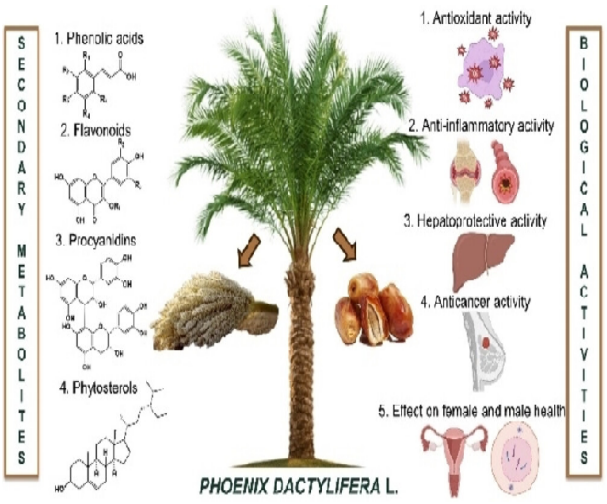

Fig (6): Biochemical and Haematological benefits (23).

6.2. Antioxidant activity

Phoenix dactylifera could exhibit antioxidant properties through its phenolics, flavonoids, and trace amounts of vitamins C, E, and GSH. These *Phoenix dactylifera* antioxidant components have the ability to either directly or indirectly interact with ROS to destroy them by either receiving or donating electrons to remove the unpaired state of ROS by promoting the activities and expression of antioxidant enzymes that prevent Protein alteration, DNA damage, and lipid peroxidation [28]. Date seeds have a

considerable amount of phenolics and exhibit strong antioxidant properties, in light of this, date seeds may present potential prospects for biological uses, functional foods and fortification to increase food items' shelf life [29]. Comparing homemade and commercial date vinegar, researchers found that the homemade product had a much higher total phenolic content and hydrogen peroxide scavenging activity [30].

Dates fermented with *Saccharomyces cerevisiae* NCIM 3495 have a Radical Scavenging Activity of 74.53% and assimilable iron of 40%. They also help to lower the risks of developing oncogenic disorders because of a weakened immune system and reduce cholesterol oxidation, which can cause diseases like arteriosclerosis and lead to cardio-respiratory disorders, among other things [31]. Experiments revealed that date seed extract is safe and guards against hepatorenal damage brought on by chemicals. The amount of proanthocyanidin and total phenol, which may reduce oxidative stress, may be attributed to this defense brought on by free radicals produced by xenobiotics -creating free radicals, restoring the physiological and histological features of the vulnerable organs in the process. According to the findings, date seeds can be a beneficial and easily accessible supply of dietary supplements, food additives, or natural antioxidants to improve quality of life [32].

6.3. Anticancer

Phoenix dactylifera comprise anti-cancer properties and promote the proliferation of probiotic bacteria. In order to treat colorectal cancer, Date palm juice should be mixed with Lactobacillus reuteri, a probiotic bacterium. This has a protective effect against colon cancer [33]. current cancer prevention initiatives aqueous extracts of palm pits after 24 hours at various concentrations were found to be effective [34]. By raising proapoptotic molecules (including p53, B-cell lymphoma 2-associated X protein, Fas, and Fas ligand) and decreasing B-cell lymphoma, ajwa date extract (15 and 20 mg/ml) inhibited human breast cancer (MCF7). Another study found that vinegars made from dates are a rich source of polyphenols that protect against oxidative stress. Polyphenol consumption reduces the risk of cancer and improves antioxidant safety in vivo [35].

The fermented date juice rich in phenolic compounds where it provides consumers with 19 phenolic acids in the form of phytochemicals, so it has a higher antioxidant activity than unfermented date juice (150–166% higher than unfermented juice). Compared to the unfermented juice, the date juice that had gone through fermentation had a far greater general acceptability during cold storage. A favorable impact on the larynx human cancer cell line (Hep-2) was also seen with the probiotic fermented date juice

employing both strains [36]. By promoting the growth of beneficial bacteria and reducing the spread of colon cancer cells, date fruit diet may improve colon health. This is an early indication that eating dates regularly could help humans maintain good bowel health and even prevent the development of colorectal cancer [37].

6.4. Antibacterial and antifungal

There is widespread scientific agreement that administering antibiotics improperly to treat infectious infections results in bacterial drug resistance. Because they serve to mitigate the negative effects of conventional medication, Currently, using natural antibacterial agents is seen to be essential [38]. Date fruit fermented with L. plantarum shown potent antifungal and antibacterial properties against A. niger, A. flavus, E. coli, and S. aureus. Dates that have been fermented have a lot of potential as useful ingredients in confections. Numerous antimicrobial metabolites discovered by 1H-NMR analysis were likely responsible for the antifungal activity [39], Secondary metabolites with antibacterial and anti-inflammatory properties include phenolic compounds [40]. After 5% (w/v) Phoenix dactylifera extract was added to yeast, scanning electron microscopy revealed weakness and deformation of the *C. albicans* cell wall.

At high concentrations of *Phoenix dactylifera* extract (20%, w/v), *C. albicans* died concurrently and suffered more severe cell lysis-related damage. *Staphylococcus aureus, Salmonella typhi, Pseudomonas aeruginosa* and *Bacillus subtilis* were the subjects of a second antibacterial investigation using Berhi date extract (20%, w/v). *Phoenix dactylifera* extract inhibited from 80 to 99% of the growth of all bacteria in nutrient broth cultures. Cell elongation caused by extract treatment significantly altered *B. subtilis.* These findings might be put to use by including *Phoenix dactylifera* extract to antibacterial medications and topical ointment production [28].

fermented palm wine contains antibacterial properties that can combat the diarrhoea-causing bacteria *Shigella dysenteriae*, *Staphylococcus aureus*, and *Escherichia coli*. Additionally, the length of the fermentation method has a big influence on the antibacterial activity. The effectiveness of palm wine in stopping these test organisms from growing increases with the length of fermentation. It is proposed that palm wine can be utilized as an alternate treatment for preventing diarrhea brought on by these bacteria when medicines are not available because it exhibits strong antibacterial activity on the test microorganisms [41].

6.5. Antibiotics and Enzymes

Date palm waste was employed in the production of enzyme processing technologies, biopolymers, biosurfactants, fermentation, and antibiotics, among other non-food applications

[42] . In the control and treatment of diarrhea, particularly in third world nations, *Phoenix dactylifera* extract after 24 hours can be utilized as an effective nutraceutical [43]. By fermenting date syrup, date-coat sugar extract, and hydrolyzed date seed containing *streptomyces rimosus* and *mobaraensis, bleomycin* and oxytetracycline were produced respectively. *Bacillus subtilis* EFRL 01, *Aspergillus niger* PC5, and *Candida guilliermondii* CGL-A10, respectively, also provided pectinase, endopectinase, and alpha amylase [44].

5. Conclusion

One of the healthiest and most complete fruits, date palm fruit is a perfect base from which to create several items with additional value for the food and nutraceutical sectors in the near future by using bioprocessing technologies. being an inexpensive and convenient source of carbohydrates and dietary fiber. Waste from date palms was utilized in non-food industries such fermentation, the synthesis of antibiotics, and enzyme processing technologies. With pronounced antioxidant, antidiabetic, anticancer, antibacterial, and cytotoxic properties, DP is a natural source of bioactive chemicals. Enhancing the health advantages of DP could be achieved by fermenting DFP with yeast species. Additionally, the fermentation of DFP increased the potential applications for date by-products. Support should be given to additional study to increase information that will help the local populace, particularly in Islamic nations where date palm fruit is abundantly available and has numerous potential health benefits.

References

[1] Hasegawa M., Yamane D., Funato K., Yoshida A. and Sambongi Y., 2018, Gamma-aminobutyric acid fermentation with date residue by a lactic acid bacterium, *Lactobacillus brevis*. Journal of bioscience and bioengineering, 125, 3, 316-9.

[2] Radia A., Boukhiar A., Kechadi K. and Benamara S., 2018, Preparation of a natural candy from date (*Phoenix dactylifera* L.), olive (*Olea europaea* L.), and carob (*Ceratonia siliqua* L.) fruits. Journal of Food Quality, 9565931.

[3] Qadir A., Shakeel F., Ali A. and Faiyazuddin M., 2020, Phytotherapeutic potential and pharmaceutical impact of *Phoenix dactylifera* (date palm): current research and future prospects, Journal of food science and technology, 57, 4, 1191-204.

[4] Saranraj P., Sivasakthivelan P. and Naveen M., 2017, Fermentation of fruit wine and its quality analysis: A review. Australian Journal of Science and Technology, 1, 2, 85-97.

[5] Saranraj P. and Ramesh C.R., 2019, Tropical fruit wines: Health aspects, International Journal of Microbiological Research, 10, 3, 94-110.

[6] Al-Snafi A.E. and Thuwaini M.M., 2023, *Phoenix dactylifera*: traditional uses, chemical constituents, nutritional benefit and therapeutic effects, Tradit Med Res, 8, 4, 20.

[7] Barh D. and Mazumdar B.C., 2008, Comparative nutritive values of palm saps before and after their partial fermentation

and effective use of wild date (*Phoenix sylvestris* Roxb.) sap in treatment of anemia, Research Journal of Medicine and Medical Sciences, 3, 2, 173-6.

[8] Ayad A.A., Williams L.L., Gad El-Rab D.A., Ayivi R., Colleran H.L., Aljaloud S. and Ibrahim S.A., 2020, A review of the chemical composition, nutritional and health benefits of dates for their potential use in energy nutrition bars for athletes, Cogent Food & Agriculture, 6, 1, 1809309.

[9] Cantadori E., Brugnoli M., Centola M., Uffredi E., Colonello A. and Gullo M., 2022, Date fruits as raw material for vinegar and non-alcoholic fermented beverages. Foods, 11, 13, 1972.

[10] Assirey E. A., 2015, Nutritional composition of fruit of 10 date palm (*Phoenix dactylifera L.*) cultivars grown in Saudi Arabia, Journal of Taibah University for science, 9, 1, 75-9.

[11] Barakat H. and Alfheeaid H.A., 2023, Date palm fruit (*Phoenix dactylifera*) and its promising potential in developing functional energy bars: Review of chemical, nutritional, functional, and sensory attributes, Nutrients, 15, 9, 2134.

[12] Alkhoori M.A., Kong A.S., Aljaafari M.N., Abushelaibi A., Erin Lim S.H., Cheng W.H., Chong C.M. and Lai K.S., 2022, Biochemical composition and biological activities of date palm (*Phoenix dactylifera* L.) seeds: a review, Biomolecules, 12, 11, 1626.

[13] Handgraaf S. and Philippe J., 2019, The Role of Sexual Hormones on the Enteroinsular Axis, Endocrine reviews, 40, 1152–1162.

[14] Salhi S., Rahim A., Chentouf M., Harrak H., Bister J.L., Hamidallah N. and El Amiri B., 2024, Reproductive Enhancement through Phytochemical Characteristics and Biological Activities of Date Palm Pollen: A Comprehensive Review on Potential Mechanism Pathways. Metabolites, 14, 3, 166.

[15] Ourradi H., Ennahli S., Martos M.V., Hernadez F., Dilorenzo C., Hssaini L., Elantari A. and Hanine H., 2021, Proximate composition of polyphenolic, phytochemical, antioxidant activity content and lipid profiles of date palm seeds oils (*Phoenix dactylifera* L.), Journal of Agriculture and Food Research, 6, 100217.

[16] Tadapaneni R.K., 2010, Effect of High Pressure Processing & Dairy on the Antioxidant Activity of Strawberry Based Beverages, PhD dissertation, Illinois Institute of Technology.

[17] Al-Alawi R.A., Al-Mashiqri J.H., Al-Nadabi J.S., Al-Shihi B.I. and Baqi Y., 2017, Date palm tree (*Phoenix dactylifera* L.): natural products and therapeutic options, Frontiers in plant science. 8, 845.

[18] Al-Okbi S.Y., 2022, Date palm as source of nutraceuticals for health promotion: a review, Current nutrition reports, 11, 4, 574-91.

[19] Paulová L., Patáková P. and Brányik T., 2013, Advanced fermentation processes, Engineering aspects of food biotechnology, 20130952, 89-110.

[20] Yafetto L., 2022, Application of solid-state fermentation by microbial biotechnology for bioprocessing of agro-industrial wastes from 1970 to 2020: A review and bibliometric analysis, Heliyon, 8, 3.

[21] Chai W.Y., Teo K.T., Tan M.K. And Tham H.J., 2022, Fermentation process control and optimization, Chemical Engineering & Technology, 45, 10, 1731-47.

[22] Echegaray N., Gullón B., Pateiro M., Amarowicz R., Misihairabgwi J.M. and Lorenzo J.M., 2023, Date fruit and its by-products as promising source of bioactive components: A review. Food Reviews International, 39, 3, 1411-32.

[23] AbouZeid E.M., Afifi A.H., Hussei R.A., Salama A.A., Youssef F.S., El-Ahmady S.H. and Ammar N.M., 2024,

Phoenix dactylifera L.: an overview of phytochemical constituents and impact on women's health, Chemistry & Biodiversity, 21, 7, e202400456.

[24] Ehimigbai R.A. and Nwosu F., 2022, Effects of *Phoenix dactylifera* Tree Fruit Extract on Cadmium Induced Renal Damage in Adult Wistar Rats, Journal of Applied Sciences and Environmental Management, 26, 5, 859-64.

[25] Onuh S.N., Ukaejiofo E,O., Achukwu P.U., Ufelle S.A., Okwuosa C.N. and Chukwuka C.J., 2012, Haemopoietic activity and effect of crude fruit extract of *Phoenix dactylifera* on peripheral blood parameters. International journal of Biology and medical research,3, 2, 1720-3.

[26] Souli A., Sebai H., Rtibi K., Chehimi L., Sakly M., Amri M. and El-Benna J., 2014, Effects of dates pulp extract and palm sap (*Phoenix dactylifera* L.) on gastrointestinal transit activity in healthy rats, Journal of medicinal food, 2014 Jul 1;17(7):782-6.

[27] Al-Sahlany S.T., Khassaf W.H., Niamah A.K. and Abd Al-Manhel A.J., 2023, Date juice addition to bio-yogurt: The effects on physicochemical and microbiological properties during storage, as well as blood parameters in vivo, Journal of the Saudi Society of Agricultural Sciences, 22, 2, 71-7.

[28] El-Far A.H., Shaheen H.M., Abdel-Daim M.M., Al Jaouni S.K. and Mousa S.A., 2016, Date palm (*Phoenix dactylifera*): protection and remedy food, Curr Trends Nutraceuticals, 1,2, 1-10.

[29] Majid A., Naz F., Bhatti S. and Phull A.R., 2023, Phenolic profile and antioxidant activities of three date seeds varieties (Phoenix Dactylifera L.) of Pakistan, Exploratory Research and Hypothesis in Medicine, 8, 3, 195-201.

[30] Hafzan Y., Saw J.W. and Fadzilah I., 2017, Physicochemical properties, total phenolic content, and antioxidant capacity of homemade and commercial date (*Phoenix dactylifera* L.) vinegar, International Food Research Journal, 24, 6.

[31] Bhusari S.I., Desai V.D., Nalavade M.L., Wadkar S.S. and Ghosh J.S., 2013, Fermentation and characterization of wine from fruits of *Phoenix dactylifera*, using Saccharomyces cerevisae NCIM 3495, International Food Research Journal, 20, 6.

[32] Ahmed A.F., Al-Qahtani J.H., Al-Yousef H.M., Al-Said M.S., Ashour A.E., Al-Sohaibani M. and Rafatullah S., Proanthocyanidin-rich date seed extract protects against chemically induced hepatorenal toxicity, Journal of medicinal food, 18, 3, 280-9.

[33] Adnan M.L. Potensi Kombinasi Bakteri Probiotik Lactobacillus reuteri dengan Sari Buah Kurma (*Phoenix dactylifera*) sebagai Terapi Penyakit Kanker Kolorektal. SCRIPTA SCORE Scientific Medical Journal. 2020 Feb 1;1(2):11.

[34] Alobaidi K. H., Mohammad F. I. and Hassan M. F., 2019, Anti-Tumor Activity of *Phoenix dactylifera* L. Pit Extracts against Hela and L20B cell lines, Res. J. Biotechnol, 14 ,196-200.

[35] Ali Z., Li J., Zhang Y., Naeem N., Younas S. and Javeed F., 2022, Dates (*phoenix dactylifera*) and date vinegar: Preventive role against various diseases and related in vivo mechanisms, Food Reviews International, 38, 4, 480-507.

[36] Mostafa H.S., Ali M.R. and Mohamed R.M., 2020, Production of a novel probiotic date juice with anti-proliferative activity against Hep-2 cancer cells. Food Science and Technology, 41, 105-15.

[37] Eid N., Enani S., Walton G., Corona G., Costabile A., Gibson G., Rowland I. and Spencer J.P., 2014, The impact of date palm fruits and their component polyphenols, on gut microbial ecology, bacterial metabolites and colon cancer cell

proliferation, Journal of nutritional science, 3, e46.
[38] Herrmann M. and Nkuiya B., 2017, Inducing optimal substitution between antibiotics under open access to the resource of antibiotic susceptibility, Health Economics, 26, 6,703-23.
[39] Muhialdin B.J., Marzlan A.A., Kadum H., Arulrajah B., Mohamad Asri N., Fathallah S. and Meor Hussin A.S., 2021, Metabolomics profiling and antimicrobial activity of fermented date fruit (Khastawi) used as functional ingredients for making Asian confectionary (Dodol), Biotechnology & Biotechnological Equipment, 35, 1, 478-86.
[40] Khlaif D.K, Kadum H. and Abod N.S., 2021, Nutritional and chemical compositions of the desert Truffle (Terfezia claveryi) in Samawa city of Iraq, IOP Conference Series: Earth and Environmental Science, 923, 1, 012050).
[41] Akinrotoye K.P., 2014, Effects of fermented palm wine on some diarrhoeagenic bacteria, Elite Research Journal of Biotechnology and Microbiology, 2,1,4-14.
[42] Aydeniz-Güneşer B., 2022, Valorization of date palm (*Phoenix dactylifera*) wastes and by-products. InMediterranean Fruits Bio-wastes: Chemistry, Functionality and Technological Applications , Springer International Publishing, 391-402.
[43] Megbo B.C., Samuel A.M. and Dio D.W., 2017, *Phoenix dactylifera* fruit: a nutraceutical agent in the treatment of diarrhea, Innovat International Journal of Medical and Pharmaceutical Sciences, 2,3.
[44] Chandrasekaran M. and Bahkali A.H., 2013, Valorization of date palm (*Phoenix dactylifera*) fruit processing by-products and wastes using bioprocess technology–Review, Saudi journal of biological sciences, 20, 2, 105-20.