

How may palm dates relieve constipation?

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Constipation is the sixth most commonly reported gastrointestinal (GI) disease and is described as:

- 1) the inability to pass less than 35g of stools daily
- 2) less than three bowel movements in seven days
- 3) a faecal water weight of less than 70%
- 4) a gastrointestinal transit time of more than five days

Constipation affects about 20% of the general population with a higher occurrence in females than males, even though the incidence of this disease increases with age. It can be classified into two main groups, functional or somatopathic constipation, with the latter being secondary to other diseases like diverticulosis or colon cancer. On the other hand, functional constipation which is sometimes referred to as primary constipation, is not caused by other diseases. It may be a result of prolonged colon passage, a poor intake of fluids or fibre, a defecation disorder, lack of exercise or even due to

medications like diuretics or opioids. Normally, once secondary causes of constipation are eliminated, the gold standard for the initial management of functional constipation is a nonpharmacological approach encompassing dietary and lifestyle interventions. This may include increasing dietary fibre or fluid intake. However, more often than not, patients may be prescribed medication with anti-constipation properties to alleviate their symptoms and increase GI motility. Such medication may include purgatives, laxatives or cathartics. All three medications have anti-constipations properties with cathartics being the most intensive in their mode of action while laxatives being the mildest.

Laxatives are the commonest class of medicines used to relieve constipation due to their stimulatory effect to defecate. This effect is brought about through the increased water and electrolyte transport into the bowel mucosa which consequently softens hardened faeces too. Laxatives are loosely classified into seven subtypes: bulk-forming, osmotic, saccharine, polyethylene glycol, stimulant, lubricant and rectal laxatives, among others. Unfortunately, since most laxatives are available as over-the-counter medication, they are often purchased to self-manage constipation resulting in low drug compliance and effectiveness. Consequently, patients are leaning more toward accessible botanical supplements and natural remedies as to modern drugs. Luckily, the native plant, *Phoenix dactylifera*, which is native to Iraq, may be one of the natural remedies we have been looking for.

Phoenix dactylifera is commonly known as palm dates or sugar palm in English. This tree has been cultivated since before 5,500BC and has easily become a dietary staple for many individuals due to its nutrient content and health benefits. This plant is a monocotyledon and belongs to the Arecaceae family with over 2,500 species. Since each part of this plant can be utilised without anything going to waste, it has attained the name the "tree of life".

P.dactylifera thrives in dry, arid regions in the presence of well-drained soil. Being a low-cost and functional food, it is grown all over the globe. However, it is cultivated in large quantities in tropical and subtropical regions, particularly in the Middle East and Southwest Asia. While Egypt, Tunisia and Saudi Arabia are among the top 10 countries that mass produce dates, Spain is Europe's main date producer.

In addition, to its rich phytochemistry and nutrient composition which are responsible for a number of health benefits like preventing colon cancer and maintaining normoglycemic blood glucose levels, date fruits may be consumed during any of the three major maturity stages out of five. These are: Khalal (pre-ripe and crunchy fruit), Rutab (ripe and soft fruit) and Tamar (sundried and dried fruit). Naturally, the chemical composition of the fruit varies during each stage of maturity.

As evidenced by a large body of literature, the laxative properties of *P.dactylifera* dates are not the result of one particular phytochemical but rather the accumulative effects brought about by various phytoconstituents ranging from minerals to phenols to fibre.

Flavonoids and phenols are both secondary plant metabolites found in various plants, vegetables and fruits. Both exhibit a range of health benefits such as acting as anti-inflammatory, anti-oxidative and anti-constipation agents. Quercetin is a prominent flavonoid in *P.dactylifera* dates and relieves constipation by manipulating signalling pathways, influencing GI hormone levels and the gut microbiome as well as altering faecal composition. Quercetin reduces the expression of aquaporin 3 (AQP3) mRNA and VIP-cAMP - PKA- AQP3 signalling pathways which are responsible for intestinal water absorption. Aquaporins play a vital role in promoting the absorption of water from the colon into the vascular system making the faeces harder. Therefore, since quercetin reduces the expression of AQP3, less water is going to be absorbed into the colon, promoting the faeces to be softer and thus preventing defecation problems. In fact, an in-vivo study demonstrated that supplementing quercetin to loperamide-induced constipation in rats, increased faecal water content and weight.

Furthermore, quercetin promotes the growth of beneficial gut flora, specifically *Bifidobacteria* and *Lactobacillus*, while inhibiting the growth of harmful bacteria like *Enterococcus* and *Fusobacterium*. In doing so, the synthesis of butyric acid and short-chain fatty acids (SCFAs) is increased which improves ileal propulsive contractions. Additionally, quercetin promotes the release of GI motility-promoting hormones (these are motilin, gastrin, substance P and acetylcholine esterase) while suppressing the production of inhibitory GI hormones like somatostatin and vasoactive intestinal peptide.

Similarly, the flavonoid caffeic acid promotes intestinal motility and colonic transit by downregulating the gene expression of nitric oxide synthase (NOS). In doing so, nitric oxide production is reduced resulting in increased intestinal peristalsis and thus enhanced GI motility. Likewise, the other flavonoids, gallic acid, ferulic acid and chlorogenic acid in *P.dactylifera*, promote GI transit too in a similar manner to quercetin by promoting the habitation of beneficial gut flora.

As most know, a low dietary fibre intake is associated with an increased risk for constipation. The recommended daily intake of dietary fibre is 25g/day and consuming 100g of *P.dactylifera* dates can contribute to up to 32% of the required daily dietary fibre. Hence the inclusion of *P.dactylifera* date fruit in one's diet may help increase faecal mass, adding to the fruit's laxative properties.

Beta-glucan is an important subunit of insoluble dietary fibre and has a very strong laxative effect. Apart from overcoming intestinal dysbiosis as observed in constipation, beta-glucan stimulates the expression of substance P, serotonin and acetylcholinesterase enhancing gut motility. It also ensures intestinal integrity by increasing the expression of tight junction proteins.

Insoluble fibre has also been reported to irritate the gut mucosa which in turn stimulates water and mucus secretion in the large colon. Similarly, soluble fibre has a significant water-holding capacity that resists dehydration resulting in the formation of a gel-like

surface in the gut. Thus, since fibre repels digestion by the gut microbiome and increases the viscosity of the GI tract, it allows stools to be excreted more smoothly and efficiently, as it adds mass, water content and weight to the faeces. Therefore, it is safe to say that the dietary fibre within *P.dactylifera* can act as a prebiotic.

P.dactylifera is a great source of magnesium (Mg^{2+}) too. Mg^{2+} can form sulfate or citrate salts, which increases water retention within the bowel due to its osmotic effect and since magnesium is not completely absorbed by the gut. This indirectly alters GI motility. Mg^{2+} also promotes peristalsis and regularises bowel movements, relieving constipation. Therefore, the anti-constipation effects of Mg^{2+} are attributed to increasing stool frequency and not stool consistency.

It is traditionally believed, especially in Eastern countries, that to obtain the maximal laxative effects in dates, one must soak 5 to 6 dates in water and leave them submerged throughout the night. The syrup produced is drunk the following morning. This should help relieve constipation and improve GI health. Although it is not yet fully understood as to why *P.dactylifera* syrups work more effectively as laxatives than their counterpart fruit, it can be speculated that the syrup produced upon soaking the dates is rich in various liberated bioactive chemicals, particularly magnesium.

Even though excessive consumption of *P.dactylifera* dates has the potential to cause kidney, bowel and stomach irritation as well as mineral and iron deficiency due to their high tannin composition, most studies have depicted this fruit as being non-toxic. In fact, doses as high as 5,000mg/kg of the aqueous date extract resulted in no mortality or toxicity symptoms being observed in the group of animals it was subjected to. Only mild liver histological changes were noted which were reversed after three weeks.

Furthermore, since quercetin is a competitive inhibitor of the enzyme CYP3A4, drugs metabolised by this enzyme should not be concurrently taken with dates. Overconsumption of soluble fibres can result in injury to the distal colon and enhancement of tumorigenesis too. This is due to the significant increase in fermentation in the proximal colon with poor delivery of health-promoting fermentation products in the distal colon. This over-fermentation may lead to toxic product production like sulphides which are toxic to colonic epithelium. Thus, the recommended dietary fibre intake shouldn't be overly exceeded to prevent unwanted harm.

In conclusion, as depicted in various studies the physiological laxative properties of *P.dactylifera* is similar to those observed in modern anti-constipation drugs. Thus, it is without a doubt that following more clinical studies, *P.dactylifera* dates may lead to the development of a plant-based laxative drug to combat constipation.

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