

● PERSPECTIVE

Beneficial effects of date palm fruits on neurodegenerative diseases

Date palm tree (*Phoenix dactylifera* L.) is an important crop, which is cultivated in many countries extending from North Africa to the Middle East, including many of the GCC (Gulf Cooperation Council) Countries (Allaith, 2008). Date palm trees have been growing for the last 5,000 years in harshest climatic condition and their fruits have been an excellent source of energy and healthy nutrition. The fruits (Dates) from these trees were believed to possess profound health-improving properties since the biblical times. Recently, science has caught up to confirm what our distant ancestors knew and what they were talking about. Hence, dates are frequently consumed among the Arabian people not only by virtue of the fact of awareness but also due to its high nutritive value and the low cost of agriculture. Fresh dates are composed of soft, easily digestible flesh and simple sugars. When eaten, they replenish energy and revitalize the body instantly. Dates are chemically composed of sugars (81–88%, mainly fructose, glucose, and sucrose), dietary fiber (~ 5–8.5%) and a small amount of protein, fat, ash, and high quantities of phenols (Elleuch et al., 2008).

The date palm fruit has been used in folk remedies for the treatment of various infectious diseases, cancer and immuno-modulatory activity (Puri et al., 2007). Thus, regular consumption of dates found to offer some protection from colon, prostate, breast, endometrial, lung, and pancreatic cancers. Dates are not only a good source of energy but also wonderful means of vitamins, and minerals. Besides nutritional value, date fruits are rich in phenolic compounds and flavonoid constituents with free radical scavenging and antioxidant

activities. Depending on the variety of dates and the degree of ripening, the ratio of both free (protocatechuic acid, vanillic acid, syringic acid, and ferulic acid) and bound phenolic acids (gallic acid, protocatechuic acid, p-hydroxybenzoic acid, vanillic acid, caffeic acid, syringic acid, p-coumaric acid, ferulic acid, and coumaric acid) varies (Al-Farsi et al., 2005; Biglari et al., 2008).

Phenolic compounds are generally good antioxidants that are known to protect cells from damage. They are known to have a preventive role against free radicals and therefore may contribute to the prevention of several age-related diseases (Scarmeas et al., 2009). The beneficial effects of dates, particularly as a good source of energy and health, have been studied extensively by many researchers all over the world. Recently, we and others have looked into the beneficial effects of dates on neurological diseases such as Alzheimer’s disease (AD), Parkinson’s disease (PD), Huntington’s disease (HD) and amyotrophic lateral sclerosis (ALS), since others have shown the beneficial effects of date palm fruits in various disease conditions (Essa et al., 2014, 2015a, b; Subash et al., 2014). Among them, AD is one of the progressive neurodegenerative disorders and a leading cause of dementia, which is characterized by cognitive and memory impairment.

In AD, the 1-42-amino-acid peptides, cleaved from a larger protein called β -amyloid precursor protein (APP) forms an amyloid-beta ($A\beta$) peptide that clusters into amyloid plaques in the blood vessels and outside the neurons of the brain leading to neural death (Chauhan et al., 1998). The regular consumption of these fruits is usually associated with lower risk of neurodegenerative disorders and better cognitive performance in the elderly (Li et al., 2007). The aqueous date fruit extract has been shown to prevent neuronal circuitry against focal cerebral ischemia (Majid et al., 2008). The amounts of phenolic, flavonoid and antioxidant contents vary from variety to variety. Therefore, our aim in this perspective is to describe the

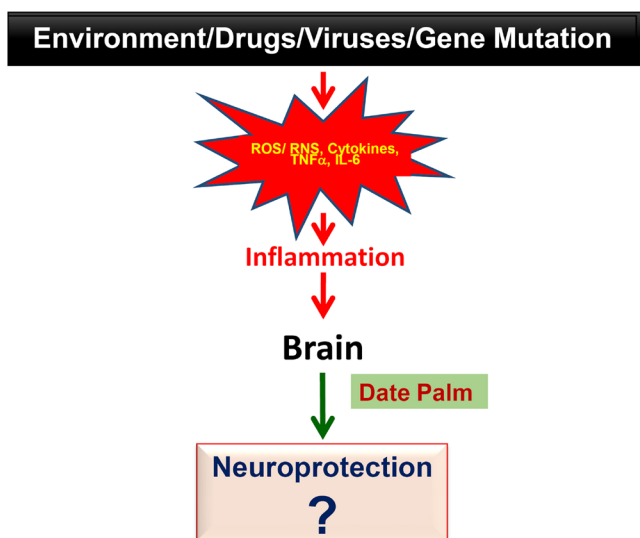


Figure 1 A schematic diagram to show whether date palm fruits can mediate neuroprotective effects against environment, drugs, viruses and mutations of genes-induced inflammation, oxidative stress and pathophysiology.

IL-6: Interleukin 6; RNS: reactive nitrogen species; ROS: reactive oxygen species; TNF α : tumor necrosis factor alpha.

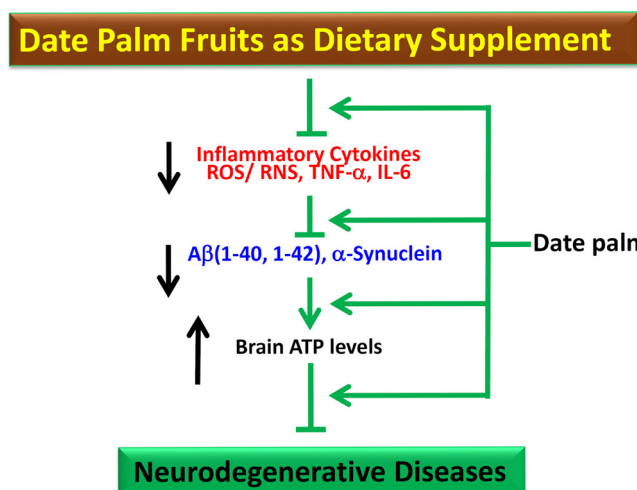


Figure 2 Date palm components (hydroxycinnamates, gallic acid, ferulic acid, monohydroxybenzoic acids, flavones and α -synuclein, and anthocyanin) inhibit proinflammatory cytokines, amyloid beta peptides and α -synuclein, and increase brain ATP concentrations, leading to the prevention of neurodegenerative diseases.

ATP: Adenosine triphosphate; IL-6: interleukin 6; RNS: reactive nitrogen species; ROS: reactive oxygen species; TNF- α : tumor necrosis factor alpha.

beneficial effects of locally grown (Oman) date palm fruits on neurodegenerative diseases. The comparative analysis of three major date palm varieties (Fardh, Rutab, and Khalas) available in Oman have shown that all the varieties had high phenolic and flavonoid contents that were found neuroprotective against 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), and quinolinic acid-induced cell death in human neurons (Subash et al., 2013). These varieties also demonstrate neuroprotective effect against the oxidative stress in a transgenic mouse model of AD (Subash et al., 2013, 2014).

The long-term (15 months) use of dietary supplementation of date fruits attenuated the levels of A β peptides, inflammatory cytokines and ATP in aged APP^{sw}/Tg2576 mice as an *in vivo* model for AD compared to wild type aged mice. The supplementation of date fruits (4%) significantly decreased pro-inflammatory cytokines such as IL-1 β , IL-2, IL-3, IL-4, IL-5, IL-6, IL-9, IL-10, TNF- α and eotaxin activity in APP^{sw}2576 transgenic mice of AD (Essa et al., 2015). In addition, putative delays in the formation of senile plaques with the decrease in brain A β ₁₋₄₀ and A β ₁₋₄₂ contents have been shown to be associated with the protective role of dates against AD. Long-term cerebral hypoperfusion in rats has been shown to cause a propensity towards anxiety and restlessness accompanied by deficits of spatial learning and memory. Post-occlusion treatment for 15 days with 100 and 300 mg/kg doses of methanolic extract of date fruits significantly reduced the levels of malondialdehyde in brain. This extract prevented neuronal necrosis as evidenced by histopathological observations in hypoperfused brains (Pujari et al., 2014).

In conclusion, the date palm fruits provide possible protection against the inflammation and oxidative stress in the brain. The mechanisms of protection may be related to the antioxidant activities of their phenolic constituents (Figures 1, 2), which clearly demonstrates the nutritional and medicinal values of this fruit. Based on the *in vivo* experimental studies and the active ingredient profiles, it can be concluded that these fruits have promising therapeutic potential against AD. However, the mechanisms by which date palm fruits display their antioxidant activities against the AD are poorly understood and necessitate an extensive investigation utilizing different varieties.

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