Title: Evaluation of Date Extract on Nerve Conduction Velocity in Male Rat

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Abstract

Introduction: neuropathy is a condition in which the peripheral nervous system is disrupted. The study of the effects of antioxidants on the performance improvement of this system is vital. This study was aimed at the investigation of the effects of date extract on nerve conduction velocity, distal latency, and wave height of the sciatic nerve in male rats.

Materials and Methods: this laboratory study used 24 male Wistar rats weighing 250 ± 10 grams, divided into the test and control group. The test group received 10% date extract, daily, at 4 ml per kilogram of body weight, for three weeks. At the beginning, nerve conduction velocity, distal latency, and wave height of the sciatic nerve were examined in all the animals, and reexamined for nerve conduction velocity at the end, three weeks later. P-values lower than 0.05 were considered significant.

Results: sciatic nerve conduction velocity and wave height were significantly increased, however, distal latency of the knee significantly declined in the test group compared to the control group.

Conclusion: The compositions of date extract accelerate electrical signal transmission.

Keywords: Date extract, Nerve conduction velocity, Male rats, Sciatic nerve
Introduction

One of the issues facing human societies, whether industrial or nonindustrial, is the irreparable damage to the peripheral nervous system. Studies have reported that, in Mumbai, damages to the peripheral nervous system have been reported in 2.4% of the people and in 8% of individuals over 55 (1-2-3). Different therapeutic methods have been adopted for peripheral nerve repair, yet, still 50 percent of these damages becomes permanent and causes disability. However, unlike the central nervous system, peripheral nervous fibers are capable of regeneration and innervation of distal targets, a process which starts almost immediately after the damage. Knowing this, it can be hypothesized that understanding the basic regulatory mechanisms for axon regeneration intended for the regulation of neuronal growth, may prove helpful for introducing new methods to accelerate and enhance nerve regeneration (4).

Dates have played a major role in human life since almost 7000 years ago, especially for the Arabs. They grow in arid and semi-arid regions (5). According to Food and Agriculture Organization of the United Nations, production, use, and industrial application of dates are on the rise (6). Dates are most produced in Egypt, followed by Saudi Arabia, Iraq, UAE, and Algeria (7). Date palms are cylindrical unbranched trunks and the entire length of the stem is also free of leaves. They only let out large leaves and pinnate leaflets on the crown at the top. Date palms are in the palm family ‘palmacae’, native to Iran, found in relatively tropical regions of Kermasnhah, Khoozestan, Fars, Kerman, Hormozgan, and Sistan and Baluchestan. Dates most likely have medicinal properties, yet still unknown (8). There are recent reports concerning the antioxidative, liver protection, anti-mutagenic, anti-tumoral, anti-inflammatory, anti-bacterial and, probably, anti-diarrheal properties as well as protection of the digestive system for this plant (9, 10, 11, 12). Date palms are in the palm family ‘palmacae’, bearing the scientific name Phoenix Dactylfer (4). Dates are used in traditional medicine for curing hoarseness, paralysis, back pain, and rheumatic pains, among others. Dates are highly important in our nutrition. The importance of dates is derived from their rich composition: carbohydrates make up 50-60% of the dried fruits (13), salts and minerals, dietary fiber, vitamins, fatty acids, amino acids, and proteins. Accordingly, dates are considered as an ideal meal, from many aspects. Dates also boost a variety of useful properties, including antioxidative, anti-mutagenic, anti-tumoral, anti-bacterial and digestive system protection effects (9, 10). They also have protective effects on the neurons, owing to compounds like polyphenol and melatonin (14). The anti-hepatotoxic effects of date extract on rat liver have already been studied (15). Studies have addressed and approved the antioxidative and anti-mutagenic effects of different species of dates (11,
There have been studies on the positive antioxidative effects of date extract in preventing diabetic neuropathy. In a study date extract treatment shows efficacy for preventing diabetic deterioration and for improving pathological parameters of diabetic neuropathy in rats, as compared with control groups. (16, 17). A study on the effects of the watery extract on pain in rats, has reported increased pain.

**Materials and Methods**: animals and lab protocols: care of laboratory animals was based on the Guide for the Care and Use of Laboratory Animals, at Kerman Neuroscience Research Center of Kerman University of medical sciences, approved by the Animal Ethics Committee. This study used male Wistar rats, weighting 200 to 300 grams.

The rats received standard diets during the study, and were kept in the animal lab in special conditions, away from pathogenic agents in a fixed temperature and normal environment (12:12 hours, light : darkness cycle).

For the purpose of statistical accuracy, intensive care was applied to minimize pain in animals and reduce the number of animals.

Animals in this study were divided into two groups of control and test (experimental). Control group received daily food and water intake without date extract and test group received food and water plus 10% date extract, 4 ml per kilogram for three weeks in the daily water intake.

It must be noted that weight of all the animals was measured along with their nerve conduction velocity (NCV), both at the beginning and the end of the intervention.

**Extracting Method**: for preparing the watery date extract, subsequent to procurement of fresh Mazafati dates from Bam orchards, the pits were removed, then, 200 grams of the date flesh was soaked in 2000 ml of distilled water for 48 hours, and later on, completely mixed by a mixer. The resulted mix, at 4 ºC, was subsequently centrifuged at 4000 rpm for 20 minutes. Then, the solution in the upper area of the tube was removed from the remaining sediment and kept in -20 ºC until use. Conducting electrodiagnostic assessments, information on control and experimental rats were done by a person blind to the experimental conditions.

**NCV Assessment and Recording**: 3 weeks after commencing the oral intake of date extract, the animals were anesthetized using Ketamin/Xylazine (50/20 mg/kg) solution. Environmental temperature was set to 25±1 throughout the study. Subsequent to shaving the legs of the animals using bipolar electrodes of AD-Instruments ML856 Power-Lab, the sciatic nerve was stimulated at
the knee and ankle, and immediately after any stimulation, the muscle's nerve potential was recorded by the unipolar electrodes attached to the sole of the hind paw. The obtained records were the biphasic responses with an initial M wave, created by the stimulation of motor fibers.

NCV (mean±SD) was calculated as the ratio of the distance between the two stimulation locations (mm) to the recording time difference between the two stimulated regions (m/s). Latency (mean±SD) was calculated as the time stimulation to recording (millisecond). The height of waves (mean±SD) was calculated to millivolts. The findings analyzed by SPSS software

Results

The experiment was conducted on 24 male Wistar rats. Average weights of the rats were 268.3±8.3 g prior to, and 275.8±11.6 g after date extract intake, which is not significant (P=0.075).

The control group, not receiving date extract, had an average weight of 266.25±10.2 at the beginning and 279.5±11.7 g at the end of the experiment, yet, although significant, weight gain difference of the two groups was not significant (P=1) (Table 1).

NCV was significantly increased from 47.2±11.5 meter/second before date extract intake to 54.1±15.2 meter/second afterwards (P=0.0000). NCV also increased in the control group: 37.2±7.6 meter/second at the beginning of the project and 39.6±8.5 meter/second at the end, indicating a significant difference (P=0.001). The increased NCV was examined in the two groups, at 2.4±2 meter/second in the control group and 6.5±4.1 meter/second in the test group, showing a significant difference (P=0.008) (Graph 1).

The difference of distal latency in knee and ankle of the cases of test and control groups at the beginning and end of the experiment was not significant (P=0.473) (Table 2).

The height of the waves in terms of millivolts, in the ankle of control group animals was 2.3±2.2 at the beginning and 2.8±2 at the end (P=0.214). The height of the waves in terms of millivolts, in the knee of control group animals was 1.6±1 at the beginning and 1.8±1 at the end (P=0.267). On the other hand, the height of the waves in terms of millivolts, in the ankle of test group animals was 2.3±2.1 at the beginning and 5.3±2.4 at the end (P=0.001). The height of the waves in terms of millivolts, in the knee of test group animals was 2.9±2.6 at the beginning and 4±1.2 at the end (P=0.181). The difference of height of waves in ankle of animals in the control and test group was significant: 0.8 for the control and 3 for the test group (P=0.020). The difference of height of waves in knee of animals in the control and test groups was similarly significant: 0.4 for the control and 1.1 for the test group (P=0.001). (Graph 2)
Discussion

According to our investigations, this study is the first to address the effects of date extract on NCV. The results of the present study shows for the first time that watery date extract considerably increases NCV. Furthermore, according to our results, it seems that these effects are induced by the accelerated myelination in the neurological unit. Conduction velocity in the central and peripheral nervous systems is an agent of myelination, as NCV is slower in unmyelinated fibers rather than the myelinated ones (9). Myelin is a multi-layer protein and lipid composition, formed by the glial cell plasma membrane. Unlike nerve cells, the remyelination speed is fast and a matter of minutes, independent of the growing age; accelerated myelination, as well as, increased myelin diameter is effective in a higher NCV (14).

In this study, the authors observed an increased wave height in the ankle of subjects in the test group after intake of watery date extract, which can be due to an increased myelin sheath activity, though this increase is mostly owed to the increased axonal activity.

The two latter findings are derived from the enhanced neural activity in the transmission of electrical signals from neurons to the muscle. An activity which is an agent of axonal diameter, which may change drastically in three weeks, being more related to increased myelin thickness or activity.

The influence of myelin in signal transmission is realized through a number of major channels. The myelin sheath insulates the axon and inhibits current leakage out of the neural route and, thus, keeps signal strength from weakening. Further, there are the Nodes of Ranvier in the periodic gaps in the myelin, which act as springboards in transmitting the signals. Date extract compositions may also accelerate the ionic activity (12).

The other activities of date palm fruit are effect on bile and fatty acids. In two studies establish that an extract made from date palm fruit acts as a co-agonist ligand for farnesoid X receptor (FXR), a nuclear receptor critical for maintaining bile acid, cholesterol, and triglyceride homeostasis (18–19). In other study shows that dates contain bioactive compounds which exert FXR-mediated regulatory effects that may contribute to the underlying molecular mechanism involved in the triglyceride-lowering action of dates. Additionally, this study identifies a new potential intestinally-mediated mechanism by which poorly-bioavailable polyphenols from dates could affect blood lipid levels without being absorbed systemically (20).

Watery date extract can influence myelin repair and growth. Making up almost half of date sugar, fructose influences the creation of fat storage in prone areas, also, owing to the many fibers of the date, it can dispose of cholesterol (21). Myelin can be one of these appropriate sites. It is a lipid tissue
composed of components with rapid regenerative and rotating capabilities, in some cases, within a few minutes. It also may affect the ion transmission of the Nodes of Ranvier (13).

The authors observed a significant increase in NCV in the control group far less than that of the test group. This increase is due to the growth of the myelin sheath, which is never-ending, though slows down after puberty. Increased NCV in the control group one month later is justifiable, as myelin synthesis is independent of age (14).

In mild lesions of the peripheral nervous system, initial unpleasant pains are often observed, spontaneous or in response to non-painful sensory stimulation (13). We believe that this unpleasant feeling is induced by impaired transmission of neural signals. This can be treated using proper medications, which help improve the activity of the peripheral nervous system, both in the myelin sheath and the axon, and probably prevent the progress of such lesions (22).

**Conclusion:** The compositions of date extract accelerate electrical signal transmission.

**Acknowledgements**

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Table 1: Weight of rats before and of after date extract intake

<table>
<thead>
<tr>
<th>Weight</th>
<th>N</th>
<th>Min</th>
<th>Max</th>
<th>Mean±St</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test1</td>
<td>12</td>
<td>260</td>
<td>280</td>
<td>268.33±8.348</td>
</tr>
<tr>
<td>Test 2</td>
<td>12</td>
<td>255</td>
<td>295</td>
<td>275.83±11.64</td>
</tr>
<tr>
<td>Cont1</td>
<td>12</td>
<td>250</td>
<td>280</td>
<td>266.25±10.25</td>
</tr>
<tr>
<td>Cont2</td>
<td>12</td>
<td>260</td>
<td>300</td>
<td>279.58±11.76</td>
</tr>
</tbody>
</table>

1 = before date extract intake, 2 = after date extract intake

Graph 1: The NCV (m/sec) of Sciatic nerve (12 rats) in Control and Test groups Before and After intake of date extract

1 = Before, 2 = After
Table 2: Distal latency (m sec) of Sciatic nerve of 12 rats at knee and ankle sites before and after intake of date extract in Test and Control groups

<table>
<thead>
<tr>
<th>Distal latency</th>
<th>N</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean±St</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test Knee1</td>
<td>12</td>
<td>2.8</td>
<td>3.3</td>
<td>2.98±0.15</td>
</tr>
<tr>
<td>Test Ankle1</td>
<td>12</td>
<td>1.8</td>
<td>2.5</td>
<td>2.07±0.18</td>
</tr>
<tr>
<td>Test Knee2</td>
<td>12</td>
<td>2.8</td>
<td>3.2</td>
<td>3.05±0.12</td>
</tr>
<tr>
<td>Test Ankle2</td>
<td>12</td>
<td>1.6</td>
<td>2.6</td>
<td>2.15±0.13</td>
</tr>
<tr>
<td>Cont Knee1</td>
<td>12</td>
<td>2.7</td>
<td>3.2</td>
<td>2.84±0.14</td>
</tr>
<tr>
<td>Cont Ankle1</td>
<td>12</td>
<td>1.4</td>
<td>2.1</td>
<td>1.75±0.23</td>
</tr>
<tr>
<td>Cont Knee2</td>
<td>12</td>
<td>2.7</td>
<td>3.3</td>
<td>2.99±0.19</td>
</tr>
<tr>
<td>Cont Ankle2</td>
<td>12</td>
<td>1.5</td>
<td>2.2</td>
<td>1.94±0.21</td>
</tr>
</tbody>
</table>

1 = Before research, 2 = After research

Graph 2: Amplitude of Sciatic nerve in Test and Control groups Before and After research

1 = Before, 2 = After