

## DRUG INFORMATION CENTER

## PHARMA INFO-LINE

**M.U.S.T. Quit Smoking Seminar**

**O**n Monday, November 12<sup>th</sup>, a seminar was held at Auditorium 116, that is located at college of pharmacy, MUST. This seminar was held under the care of Mr. Khaled El-Toukhy; *Chancellor, Chairman of the Board of Trustees* and Prof. Mohamed Raafat; the president of MUST University, as a part of MUST smoke-free campaign. The campaign that was initially called by professor M.F. El Meligi; Dean of Pharmacy College, MUST.

The seminar was composed of two presentations that were made by two outstanding professors in the field of clinical pharmacology;

Prof. Ezz El Denshary, Professor of Pharmacology and Toxicology, Cairo University and Misr University; and Professor Haider Ghaleb, Professor of Pharmacology, Faculty of Medicine, Cairo University and recently has joined the consultants board of College of Pharmacy- MUST.

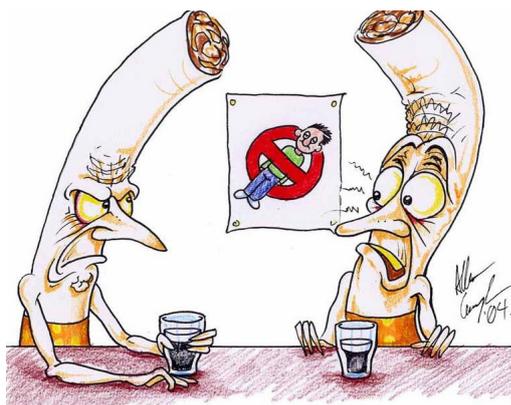
In the first presentation; Prof. El Denshary focused mainly on health and socio-economical burdens of smoking on the community. After enumerating all smoking consequences, he provided the practical ways to encounter this bad habit in the Egyptian community. The solutions that were provided by him represented the core elements in the

smoke-free campaign such as; organization of series of educational meetings in order to increase Egyptian population awareness on the dangers of smoking at different levels; from pupils at schools, to youth at sports and cultural clubs, in addition to organization of training programs for pharmacy students in order to be ambassadors for the campaign in the campus.

In the second presentation professor Ghaleb focused on the compelling reasons for smoking and the pharmacological background for them. One of the important reasons he said "feel of rewards gaining" that is produced as a sequence of neuro-chemical processes that takes place in the brain. He also promised to provide a guideline that will help healthcare professionals to manage smoking cessation in individuals who wish to quit smoking.

The seminar was an interactive that elicited many comments as well as personal experiences. One of these interesting comments was by Dr. ElHakeem professor of pharmacology at MUST and an ex-heavy smoker who said that strong will was his magic key for quitting smoking.

You can download the whole seminar from the Drug information newsletter page at; <http://www.must.edu.eg/Pharmacy/lectures.php>



## INSIDE THIS ISSUE:

***Is it possible that Karkadeh replaces anti-hypertensive medications?***

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**Article summary**

- Smoking has both health and socio-economic burdens.
- Feel of reward gaining is a compelling reason for continuous smoking.
- Strong will is needed in order to quit smoking.

## Is it possible that Karkadeh replaces the antihypertensive medications?

Hibiscus Sabdariffa, also known as Roselle is originally native to tropical Africa but today grows throughout many tropical areas. It produces elegant red flowers. The herb has many common names all over the world such as roselle, sour tea and in Egypt it is called Karkadeh (كر كديه). Historically Karkadeh had a multi-use in Africa and neighboring tropical countries; its fragrant flowers are used in sachets and perfumes, in areas of northern Nigeria, this plant is used to treat constipation. The fleshy red calyx is used in the preparation of jams, jellies, cold and warm teas and drinks. The leaves are used like spinach.

In Egypt the plant is widely used for the treatment of cardiac and nerve diseases and is described as a diuretic. In Iran as well as in Egypt drinking karkadeh tea is believed to lower blood pressure in hypertension[1]. In Western countries, hibiscus flowers often are found as components of herbal tea mixtures. Karkadeh seed products (ie, karkadeh defatted flour, protein concentrate, protein isolate) have been studied for their nutritional and functional value[2].

Hibiscus sabdariffa was subjected to many phyto-chemical studies in order to identify its active constituents. Many ingredients and chemical entities have been separated from the herb such as; fruit acids which give its sour taste, anthocyanins which give the intense red color, flavonoids and finally mucillages[3].

There are numerous pharmacologic studies in the literature, which were performed on both aqueous and alcoholic extracts of hibiscus and showed the following effects;

- »Smooth muscle relaxation as seen in rabbit aortic strip[4] and in rat ileal strip[5].
- »Antioxidant with hepatocyte protection[6] and antimutagenic activity[7]
- »Antipyretic and antinociceptive effects[8].
- »Diuretic and uricosuric effects [9, 10].
- »Cholesterol lowering and anti-atherogenic effects[11].
- »Blood pressure lowering effect [12-15].

The mechanism and the responsible active ingredient/(s) for blood pressure lowering effect of karkadeh are not yet fully understood. Many mechanisms were postulated based on its different pharmacologic actions such as; vaso-

dilatation by cholinergic or histaminergic actions [12, 13], inhibition of angiotensin I converting enzyme ACE [16], and eventually by inducing diuresis[15, 17].

Till now only few clinical trials were designed to address the hypotensive effect on humans, in the following paragraphs you are going to read summaries of these clinical studies;

In the first clinical study; **Haji Faraji et al** [18] have conducted a sequential randomized single-blind, controlled clinical trial in which; they initially randomly assigned 80 patients with high blood pressure; systolic blood pressure (SBP)160-180 mmHg and/or diastolic blood pressure (DBP) 100-114 mmHg, Who use two or less antihypertensive drugs and with no secondary hypertension HTN or underlying diseases, such as cardiovascular abnormalities, thyroid diseases, or diabetes.

All patients had to stop their treatments one week before being randomly assigned to drink a decoction of hibiscus tea (experiment) or ordinary tea (control) one hour at least before measuring their blood pressure. Blood pressure measurements were done before the study and at days 4, 8, 12 of using the tea and 3 days after stopping its use (study period 15 days).

Of the 80 patients who were initially recruited only 54 patients completed the study (31 in the experiment and 23 in the control). The authors reported significant lowerings of the systolic blood pressure(11.2%) and diastolic pressure (10.7%) in the experimental group 12 days after beginning the treatment, as compared with the first day. In addition the difference between the systolic blood pressures of the two groups was significant, as was the difference of the diastolic pressures. Three days after stopping the treatment, diastolic blood pressure was elevated by 6.2%, and systolic pressure was elevated by 5.6% in the experimental group. However, the systolic blood pressure decreased 0.6% and diastolic blood pressure increased by 0.4% in the control group. This difference between the two groups was also significant[18].

The study had some flaws since the distribution of patients according to their gender (male: female) was not the same between the 2 study-groups (in the experimental group, 45% of the patients were male and 55% were female, while in the control group, 30% of the patients were male and 70% were female). Furthermore; twenty six (26) patients withdrew from the study before using the experiment or control tea due to rise in their

blood pressure and most of them were in the control group (17), which may tend to disrupt the analysis, whereas more patients with worse conditions in the control group were removed from the analysis, therefore mitigating the difference in blood lowering between the 2 groups. This study however, proved that Karkadeh has potential antihypertensive effect as traditionally believed by the public and as shown in previous results of both in vitro and in vivo pharmacologic studies.

The second study was conducted by **Herrera et al** [19], who compared the antihypertensive effectiveness and tolerability of a standardized extract from *Hibiscus sabdariffa* with captopril. The clinical trial which was both controlled and randomized have included 90 patients, their age ranged from 30 to 80 years old and who were diagnosed hypertensive without using antihypertensive treatment for at least 1 month before the study.

The experimental procedure consisted of once daily administration of water infusion of *H. sabdariffa* that was prepared using 10 g of the dry calyx, which is equivalent to 9.6 mg anthocyanins content, while the control group had to take captopril 25 mg tablets twice a day. The study continued for 4 weeks.

The outcome variables were tolerability, therapeutic effectiveness (diastolic reduction  $\times 10$  mm Hg). Other variable in the experimental group was urinary electrolytes modification.

Fifteen (15) patients withdrew from the study due to non-medical reasons; so, the analysis included 39 and 36 patients from the experimental and control group, respectively.

The authors reported that *H. sabdariffa* was able to significantly decrease the systolic blood pressure (BP) from 139.05 to 123.73 mm Hg and the diastolic BP from 90.81 to 79.52 mm Hg. At the end of the study, there were no significant differences between the BP detected in both treatment groups.

The rates of therapeutic effectiveness did not significantly differ and were 0.7895 and 0.8438 with *H. sabdariffa* and captopril, respectively. The tolerability was 100% for both treatments.

A natriuretic effect was observed with the experimental treatment. The authors concluded that their data confirm that the *H. sabdariffa* extract, standardized on 9.6 mg of total anthocyanins, and captopril 50 mg/day, did not show significant differences relative to hypotensive effect, antihypertensive effectiveness, and tolerability [19].

Although this study has some variation in patient distribution between the 2 study groups, where more smokers and patients with higher SBP were included in the captopril group than in the experi-

ment group. However, the study has an advantage over the previous one in that the extract of hibiscus had quantified amount of the active ingredients namely anthocyanins which were postulated to produce the hypotensive effect. This study also showed that hibiscus tea has blood pressure lowering effect on human subjects.

The third study by **Herrera et al** [20], which was a randomized, controlled, double-blind study has included 193 patients that were 25-61 years old with hypertension stage 1 or 2, and have not received treatment at least during the previous month before the study. The patients were randomly assigned to receive aluminum envelopes that were identical in shape and contained either *H. sabdariffa* dried extract that contains 250 mg of total anthocyanins to be dissolved in 250 ml and ingested daily for 4 weeks (experimental group) or lisinopril 10 mg that was mixed with the appropriate pharmaceutical vehicle to follow the same procedure (control group). Outcome variables included effectiveness; measured as  $\geq 10$  mmHg reduction in DBP, safety, expressed as absence of pathological modification in the biochemical tests of hepatic and renal function, tolerability; absence of severe adverse effects and finally serum electrolyte and ACE activity. Exclusion criteria included; patients with nephropathy, heart or hepatic diseases, cancer, non-controlled diabetes mellitus, pregnancy, breast feeding, or evidence of secondary HTN.

The authors reported that experimental treatment decreased blood pressure significantly from 146.48/97.77 to 129.89/85.96 mm Hg, reaching an absolute reduction of 17.14/11.97 mmHg. However, it was significantly less than that obtained with lisinopril which had an absolute reduction of 23.31/15.39 mmHg. The other parameters such as safety and tolerability were comparable between the study groups.

The authors concluded that the blood pressure lowering effect by hibiscus can be via two modes of actions which are; diuresis and ACE inhibition [20].

### **Conclusion:**

*Hibiscus sabdariffa* (karkadeh) is widely consumed by the Egyptians both as cold and hot drinks; it is believed to lower the blood pressure and to have a calming effect on the nervous system. Pharmacologic studies have provided many effects of *H. sabdariffa* extract and blood pressure lowering effect was one of them. Till today there are only three clinical studies in the literature that have supported this effect. The mecha-

nism by which karkadeh lowers the blood pressure is not fully understood. However it may be produced by diuresis or ACE inhibition as it has been prescribed in one of these clinical studies.

It is important to emphasize that, until we have full knowledge of the active ingredient that is responsible for the hypotensive effect and determination of dose- response effect; karkadeh should never replace antihypertensive medications, nor is recommended for patients who are on anti-hypertensive treatment, as severe hypotension may occur due to additive hypotensive effect with karkadeh. However, karkadeh may have role in pre-hypertensive individuals who have no risk factors and those who are going to try changing life-style before anti-HTN treatment is prescribed to them. This group of people can drink the infusion as a part of their diet changes while their blood pressure is being closely monitored.

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