Hibiscus rosa-sinensis L. (*red Hibiscus*) Tea, Can It Be Used as A Home-Remedy to Control Diabetes and Hypercholesterolemia?

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Abstract

According to traditional medicine, Hibiscus is used to treat hypertension, heart diseases and many other ailments. Commercially available Hibiscus tea is prepared with *H. sabdariffa* and is expensive. *H. rosasinensis* is the common variety which is abundant in tropical home-gardens, however the scientific data are lacking on the effects. The present review focuses on the available scientific data on the effects of *H. rosasinensis* on controlling diabetes and hypercholesterolemia. The endeavour was to identify whether *H. rosasinensis* flower petals as a 'tea' is effective for diabetic and hypercholesterolemic patients. Medical databases such as MEDLINE, BMC, BMJ, research gate, Mendelay literature search database, Google scholar and the general engine Google were searched from November 2018 to April 2019. Search was carried out using keywords such as "*Hibiscus rosasinensis*", "antidiabetic effects", "antihyperlipidemic effects", "toxic effects", "anti-inflammatory effects", "phytochemicals in Hibiscus" etc. Data were critically analyzed to assess whether the effective doses of the research studies on a par with the doses present in *H. rosasinensis* teas. We found thirty-nine journal articles fulfilled the criteria. The data were categorized and extracted on uses of *H. rosasinensis*, anti-diabetic effects, anti-inflammatory effects, anti-hypercholesterolemic effects and its phytochemicals. The review revealed that the dose of *H. rosasinensis* petals present in a home-made Hibiscus tea is theoretically sufficient to elicit anti-hyperglycemic and anti-hyperlipidemic effects. Home-made Hibiscus tea is effective in controlling diabetes and hypercholesterolemia without causing acute toxicity.

Keywords: *Hibiscus rosasinensis*; *Hibiscus sabdariffa*; diabetes; hypercholesterolemia.

INTRODUCTION

The trend of the use of herbal remedies is rapidly growing globally (Ekor & Pistelli, 2013). Based on 2002 data, almost four billion people in the world relied on herbal remedies for primary health issues(Mukherjee, 2002). Although the beneficial effects of these herbal remedies on health problems have been observed and experienced by humans for thousands of years, yet minimum scientific data are available on these treatments (Ekor & Pistelli, 2013). Lack of data on the mode of action, potential adverse reactions, contraindications and interactions with existing Western medical treatments has restricted these products from being 'competitive leading herbal supplements' in the market.

Hibiscus is a family of flowering plants which the leaves and the red flower petals are used as herbal remedies by most people in the world. Yet data are scarce on the effects of different varieties. Consumption of tea made of flower petals of Hibiscus family is being practiced by a large number of patients in the world to control hypertension and hyperlipidemia (Haji Faraji & Haji Tarkhani, 1999; McKay et al, 2010) thus Hibiscus tea is commercially available in international markets. To prepare Hibiscus tea, a variety of flowers which are belonged to Hibiscus family is used. *Hibiscus sabdariffa* is the mostly consuming variety which also has scientifically proven hypotensive and hypolipidemic effects (Haji Faraji & Haji Tarkhani, 1999; McKay et al., 2010). However, *Hibiscus rosasinensis* is the most common, easily cultivated plant which is accessible to most people in the world as it is grown massively in tropics and sub-tropics (it can be cultivated in glass chambers in cold weathers as it does not tolerate temperatures below 10°C). Aqueous extract of *Hibiscus rosasinensis* red flower petals is a common herbal home-remedy consumed by people in Asian countries however, has minimum scientific data to prove the effects on humans. This plant is a glabrous shrub cultivated as an ornamental plant. Among the different colors, red flowered variety is mostly used as a herbal remedy (Jadhav et al., 2009).

Due to universal availability and good palatability, herbal home-made tea could be prepared with the petals of *Hibiscus rosasinensis* with a minimum preparation time. Prior a study on the effects of *Hibiscus rosasinensis* tea on humans, the present review mainly focuses on the effects of this flower on diabetic and hypercholesterolemic animals.

METHODS

Several medical databases such as MEDLINE, BMC, BMJ, research gate, Mendelay literature search database, Google scholar and the general engine Google were searched from November 2018 to April 2019. Some full articles were accessed through Hinari gateway. We used categorized search using keywords such as "Hibiscus rosasinensis", "antidiabetic effects", "antihyperlipidemic effects", "toxic effects", "anti-inflammatory effects", "phytochemicals in Hibiscus" etc.

We included trials conducted with animals and humans that had examined the effectiveness of *Hibiscus rosasinensis* and safety in the treatment of hyperglycemia and hyperlipidemia. As the review focuses on the effectiveness of Hibiscus tea, the initial endeavour was to review the studies carried out only with water extracts of the flower petals and to exclude the studies carried out with other solvent extraction methods. However, due to scarcity of published data, studies conducted with other solvent extraction methods were also included. Researches carried out with parts of the Hibiscus plant except for petals were excluded.

After gathering the relevant articles, we cross-referenced to see the validity and traced back to the original articles to avoid any plagiarism. Most commonly discussed most recent research findings in the original articles were included to conclude this review.

The articles were categorized to extract data on uses of *H. rosasinensis* by humans, anti-diabetic effects, anti-inflammatory effects, anti-hypercholesterolemic effects and phytochemicals in *H. rosasinensis*. Data were critically analyzed to assess whether the effective doses of the research studies on a par with the doses present in *H. rosasinensis* teas.

Description of the Plant

Different names used for this plant in different countries are given in the first volume of the "Medicinal Plants of the World" by Ivan A. Ross (Ross, 2003).

The plant is a shrub with long slender branches of about 6 m tall. The Flowers are borne singly at the apexes or ends of the branches, on long stalks. Flowers possess colorful overlapping petals (Ross, 2003).

Classification:

Kingdom   : Plantae
Clade   : Angiosperms
Clade   : Eudicots
Clade   : Rosids
Order   : Malvales
Family   : Malvaceae
Genus   : Hibiscus
Species   : H. rosa-sinensis

Evidence for the Use of the *H. rosasinensis* Flower by Humans

To regulate the menstrual cycle, females of Bangladesh use a decoction of the flower petals with green beetle nut. Hot water extract of flowers is used by Chinese as an emmenagogue and a tonic. Flower extract is used by East Indies to regulate menstrual cycle and to produce abortion. In Fiji, hot water extract of flowers and leaves is used orally to ease childbirths and the infusion of dried flower is used to aid digestion. People in Haiti use decoction of flowers to cure flu and cough while Hawaiians eat flowers to produce lactation. Decoction of dried flowers is used by Indians for abortion and the hot water extraction of flowers as a contraceptive (Ross, 2003). Flowers, crushed with sugar, are used in Indian folk medicine to control excessive uterine bleeding. Ancient Indian medicinal literature reveals the use of Hibiscus flowers for heart diseases. Flowers have cooling and soothing effects, anti-inflammatory effects and emmenagogue effects. Petals are used to stimulate hair growth, to prevent premature graying and hair loss and used as a hair conditioner (Linn et al, 2009; Upadhyay et al, 2011). In Sri Lankan Ayurveda medicine, flowers are used to treat anaemia, constipation and to stimulate hair growth (*Ayurvedic Medicinal Plants of Sri Lanka*, n.d.).

Antidiabetic Effects

A study conducted in India with Alloxan induced diabetic Wistar rats revealed that the ethanolic extract of *H. rosasinensis* elicits acute hypoglycemic effects (1, 3, 5 h) and sub-acute (1, 3, 5, 7 days) hypoglycemic effects at doses of 250 mg/kg and 500 mg/kg (Venkatesh et al, 2008). Thus, to obtain this effect, a human should consume around 40 mg/kg BW of dried ethanolic extract of *H. rosasinensis* (Reagan-Shaw et al, 2008). Required weight of dried petals to make Hibiscus tea to obtain the above effect will be much higher.

When Streptozotocine induced diabetic female Wistar rats were mated, and treated orally with aqueous extract of *Hibiscus rosa-sinensis* during pregnancy, an increased maternal and fetal weights, reduced atherogenic index, coronary artery risk index and reduced pre-implantation loss rate were observed compared to the untreated diabetic group (Afiune et al., 2017).

A study conducted by Bhaskar and Vidhya revealed that administration of aqueous extract of *H. rosasinensis* flowers at a oral dosage of 500 mg/kg to normal rats, lowered the postprandial (2hr) blood glucose level significantly (p<0.001) after an oral glucose load. Moreover, administration of the extract at the same dose over 21 days, significantly lowered the fasting blood glucose level (p<0.001), glycosilated hemoglobin level and serum lipid levels of STZ induced diabetic Wistar rats, compared to the control group, although a significant change in insulin levels were not exhibited (Bhaskar & Vidhya, 2012).

Scientific data is scarce on human studies of the effect of *H. rosasinensis* flowers. However, data on human studies are available for tea made with *H. sabdariffa*, a similar flower variety to *H. rosasinensis*. *H. sabdariffa* is the variety commonly used in manufacturing Hibiscus tea. Arabic people used to consume Karkadeh tea made from *H. sabdariffa* mainly after meals. In a study, this tea was prepared by boiling 10g of dried petals in 500mL of water for 60 minutes. Final volume was 250 mL which was refrigerated at 4°C until consumption. This tea elicited a slow rise in blood glucose level compared to English breakfast tea, after a high glycemic meal. Conversely, the meal with Karkadeh tea showed a 20% higher Area Under the Curve (AUC) compared to the meal with English breakfast tea (Harrison et al, 2009) indicating the slow glucose absorption.

The only human-study carried out with *H. rosasinensis* flowers has been conducted for 60 days providing 2g of *Hibiscus rosasinensis* flower powder incorporated in to mathri (an Indian rotti variety) to type 2 diabetes patients. This study revealed a significant decrease in mean fasting blood glucose, post prandial blood glucose level, mean glycosylated Hb level, mean total cholesterol, triglyceride level, total LDL and total VLDL cholesterol level (Sharma et al, 2016). However, the study has been carried out with 6 subjects in each test and control groups and the groups have not been crossed over.

Anti-inflammatory Effect

Type 2 diabetes mellitus is an inflammatory disease (Donath & Shoelson, 2011) thus the herbs which possess anti-inflammatory effects might be beneficial in controlling diabetes. Ethanolic extract of *H. rosasinensis* showed the significant anti-inflammatory activity at doses of 125, 250 and 500 mg/kg on carrageenin induced paw edema, cotton pellet induced granuloma and xylene induced mice ear edema (Birari et al., 2009). Ethanolic extract of white Hibiscus (*Hibiscus rosa-sinensis* var alba) elicits more potent anti-inflammatory effects over red Hibiscus (*Hibiscus rosa-sinensis* L) with doses of 50 and 100 mg/kg and elicited a significant reduction (P<0.05) in polymorphonuclear leukocytes infiltration (Raduan et al., 2013).

Antihypercholesterolemic Effects

A significant improvement in dyslipidemia caused due to diabetes mellitus was observed in Alloxan induced diabetic Wistar rats with oral doses of 50, 100, 200 mg/kg of Hydroalcoholic extract (70%) of flowers of *Hibiscus rosasinensis*, administered for 4 weeks. Researchers reported a significant reduction in total cholesterol, triglycerides, VLDL, LDL and elevation in HDL levels (M Pethe & Guptha, 2011).

A decrease in the triglycerides and ALT levels were observed in pregnant diabetic Wistar rats fed with *H. rosasinensis* aqueous extract at a dose of 100 mg/kg from day 0 to 7 of pregnancy, 200 mg/kg from day 8 to 14 and 400 mg/kg from day 15 to 20. However, no effect on glycemia was observed in this study (Silva et al., 2015).

When alloxan induced diabetes rats were administered with hydroalcoholic extract (70%) of Hibiscus rosa-sinensis, at doses of 50,100 and 200 mg/kg BW for 4 weeks, a significant improvement in diabetes induced dyslipidemia was observed by the researchers with a significant decrease in total cholesterol, triglycerides, VLDL, LDL and elevation in HDL levels (M Pethe & Guptha, 2011). Further, significant anti-diabetic effects which were comparable to glibenclamide and sulphonylurea were observed with the same dosed administered for 28 days. Histopathological studies showed an increase in the size and number of islets, diameter of the islet cells and decrease in the necrosis and atrophy of the islets (Pethe et al, 2017). After administrating ethanolic Hibiscus flower extract for 21 days, a maximum blood glucose lowering of 41-46% and total cholesterol and serum triglycerides lowering of 22 and 30%, respectively were observed with Streptozotocine induced diabetic rats. The effect was comparable to Glibenclamide, however with no increase in insulin level (Sachdewa & Khemani, 2003).

Furthermore, anthocyanin compounds delphini-din-3-O-sambubioside and cyanidin-3-O-sambubioside, extracted from *Hibiscus rosasinensis* petals elicited potent competitive ACE inhibitor effects agreeing to the use of *H. rosasinensis* petal extracts to treat hypertension in folk medicine (Ojeda et al., 2010).

Moreover, Khan et al. (2011) revealed that the chronic use of ethanolic and chloroform extracts of *H. rosasinensis* petals has anti-anxiety effects without producing any CNS depression signs in experimental rats (Mohammed J et al., 2011).

Phytochemicals in Flower on Blood Glucose and Serum Cholesterol

Scientific data revels that the edible parts of the *H. rosasinensis* flowers contain 89.8% moisture, 0.064% nitrogen, 0.36% fat, 1.56% crude fibre.

Moreover, flower extract contains tannins (7.5±0.20 %), phenols (0.678±0.14%) and alkaloids (0.51±0.16 %) while the total phenol content in flowers was 735±46 mg gallic acid equivalent /100g. The four main types of flavanoids in petals are rutin, quercetin, kaempferol and myricetin (Purushothaman, Meenatchi, S, Sundaram, & Saravanan, 2018). Petals contain various flavones such as quercetin-3-di-0-beta-D-glucoside, quercetin-3-7-di-0-beta-D-glucoside, cholesterol, campesterol, quercetin-3-0-beta-D-sophorotrioside, ß-sitosterol10, kaempferol-3-0-beta-D-xylosyl-glucoside19, catalase13. Red and magenta colour flower petals possessed dark-purplish dye, anthocyanin pigment and cyanidin diglucoside (Subramanium & Nair, 1972; *Wealth of India*, 1997) along with proanthocyanidins (Nakamura et al, 1990). Another study reveals the presence of terpenoids in flower petals (Patel & Adhav, 2016). All these compounds elicit antioxidant properties, thus the antioxidant capacity of the petals were significantly high [ascorbic acid equivalent antioxidant capacity (AEAC): 640 ± 56 mg ascorbic acid /100g; total anthocyanin content (TAC): 284 ± 17 mg cyanidin-3-glucoside equivalent/100g; ferric-reducing power (FRP): 4.0 ± 0.3 mg gallic acid equivalent /100g (SK, Lim, & Chan, 2009)]. In another study, aqueous extract of Hibiscus elicited high tannin and anthocyanin contents, and possessed high ferric reducing antioxidant power (Mak et al., 2013). Further, fresh flowers of *Hibiscus rosasinensis* possess 0.30-0.50 v/w % of essential oils.

Most of the beneficial effects of this flower variety could be due to the presence of antioxidants, which play a key role in controlling diabetes and hypercholesterolemia. Phenolic compounds in tea inhibit α amylase and α glucosidase enzymes, the key enzymes of carbohydrate digestion (Hara & Honda, 1990). Furthermore, polyphenolics in tea inhibit glucose uptake by Intestinal Caco-2 cells (Johnston, 2005). Tannic acid, a major compound of tannins and alkaloids, stimulates the translocation of glucose transporters (GLUT 4) and increase phosphorylation of insulin receptors thus increasing glucose clearance from blood and activating insulin action respectively (Li et al., 2005). The whole plant of *Hibiscus rosasinensis* increase insulin secretion from the pancreatic beta cells, probably by the actions exerted by alkaloids, flavanoids and terpenoids (Mishra, 2009).

Owing to the above actions on GLUT 4 receptors and insulin receptors, polyphenolic compounds might increase deposition of excess glucose in adipose tissues as fat, increase uptake of triglycerides from adipose tissues by activating lipoprotein lipase and inhibit hormone sensitive lipase which involve in adipolysis. Summative action will be the decrease of circulatory triglycerides and phospholipids. Further, Anthocyanins in *Hibiscus sadariffa* inhibit Angiotensin Converting Enzyme (ACE) by competing with the substrate of the enzyme, thereby controls hypertension (Ojeda et al., 2010).

Terpenoids are present in many herbal plants which can modulate activities of ligand-dependent transcription factors [peroxisome proliferator-activated receptors (PPARs)] and thus can prevent obesity-induced metabolic disorders, such as type 2 diabetes, hyperlipidaemia, insulin resistance, and cardiovascular diseases (Goto et al., 2010).

Quantitative analyses have revealed that the aqueous extract of *Hibiscus rosasinensis* flower petals have high amounts of tannins and anthocyanin thus show high ferric reducing antioxidant power. Among the phenols, flavonoids, tannins, flavonol and anthocyanins are the most potent antioxidants in Hibiscus (Mak et al., 2013) thus it can be hypothesized that the above beneficial health effects also could be obtained by Hibiscus tea.

However, all above beneficial effects have been observed with isolated polyphenolic compounds. Therefore, it is not clear whether a tea made from the herbal plant or flower will exert the same effect. Although data on animal studies are available to prove the anti-hyperglycemic and anti-hyperlipidemic effects of *Hibiscus rosasinensis* extracts, human studies to observe the activity of these compounds in human body, are yet to be carried out.

Does The Dose in *Hibiscus rosasinensis* Tea Is Sufficient to Cause The antihyperglycemic and Antihyperlipidemic Effects?

The above evidences show that the *H. rosasinensis* could be beneficial as a tea, after meals in terms of controlling postprandial blood glucose level, which is a key goal to minimize diabetes related macro and micro-vascular complications. However, in most of the animal studies, the beneficial effects were obtained with the powder of the dried or evaporated solvent extracts of the petals, which the concentration of the active compounds ought to be higher than the amounts present in a tea. As a commercially available tea bag weighs 2 – 2.5g, this amount might not be sufficient to provide the beneficial

effects as shown in research. Yet, the study conducted by Sharma et al. in 2016, with diabetic patients, emphasizes the presence of anti-hyperglycemic effect of the petal powder (2 g) when incorporated in to a food (Sharma et al., 2016). Furthermore, to obtain the similar effects observed in animal studies (studies using rats), only one sixth of the animal dose has to be given to humans. Therefore, present review reveals the necessity of further studies on antihyperglycemic and antihyperlipidemic effects of *Hibiscus rosasinensis* tea.

Toxic Effects
Antifertility Effects:
A study was conducted to observe the effect of *H. rosasinensis* on diabetes during pregnancy. Dried and powdered flower petals (20 g) were boiled in 1 L of water for 5 minutes, filtered and evaporated in a rotary evaporator to obtain the test samples. STZ induced diabetic female rats were administered with an initial dose of 100 mg/kg/day of the *H. rosasinensis* extract, from day 0 until the 7th day of pregnancy (implantation period). The dose was increased to 200 mg/kg/day from day 8 to 14 of pregnancy (embryonic period), and to 400 mg/kg/day from day 15 to 20 (fetal period). The study revealed beneficial effects of the flower extract on diabetic pregnant rats and their offspring with no effect on non-diabetic pregnant rats. The non-diabetic treated group elicited decreased high density lipoprotein cholesterol, increased atherogenic index (AI) and coronary artery risk index (CRI), and increased pre-implantation loss rate compared to the non-diabetic untreated group. Treatment has not shown toxicity, however, could be deleterious to cardio vascular system and reproductive functions. Therefore, the researchers indicate that the indiscriminate intake of *H. rosasinensis* extract may be harmful to healthy individuals and further emphasize that this extract should be completely avoided during pregnancy (Afiune et al., 2017).

Extractive value of water soluble extractives of *H. rosasinensis* is 5.3% (Al-snafi, 2018). Therefore, according to the previous study, from 20 g of dried petals 1.06 g of water soluble extractives could be gained. The highest water soluble extractives dose/ day which caused the deleterious effects on rats, was 400 mg/kg/day. However, the dose for humans which causes same effect will be six times lower than that of rats (11). Therefore, the deleterious water soluble extractives dose will be 3.3g/day. This amount is present in 62.9 g of dried petals. A tea bag contains 2-2.5 g of dried petals which is significantly lower than the toxic dose.

Acute Toxic Effects:
When powder of the methanolic extract of *H. rosasinensis* was administered to rats, in 100, 200, 400, and 800 doses, no significant changes in behavior, skin effect, breathing, defecation, postural abnormalities, impairment in food intake and water consumption and yellowing or loss of hair were observed. No changes were observed for one week. However, 20% mortality was observed with a 1600 mg/kg dose (Meena et al, 2014). Ethanol soluble extractive value for *H. rosasinensis* was 2.6% (Al-snafi, 2018). Thus by considering the ratio of the dose for rats and humans, to obtain a 20% mortality rate, 13 g of ethanol soluble extractives have to be consumed by a 50 kg human. This amount is present in 500 g of dried petals. A tea bag contains 2-2.5 g of dried petals which is significantly lower than the toxic dose.

Genotoxic Effects:
Genotoxicity was not observed with the flower extract, therefore *Hibiscus rosasinensis* could be used as a safe pharmaceutical material (Meena et al., 2014).

Cytotoxic Effects:
When a decoction was prepared with 15 g of dried and milled Hibiscus petals and diluted to 5g/L and 10g/L, it showed a reduction in mitotic index for *L Allium cepa L.*, significantly. Therefore, *H. sinensis* contains anti-mitotic constituents which block anywhere of the cell cycle (Ali, 2010). These concentrations are similar to 1.25g and 2.5 g of petals in a tea cup of 250 mL respectively. However, the study was carried out with plant materials and may not be applied to the human body.

Chronic toxic effects of *Hibiscus rosasinensis* flower extract have not been reported yet, although tea and drinks made from *Hibiscus rosasinensis* flower petals have been used globally from ancient times as a home remedy and a beverage.

CONCLUSION

The dose of *H. rosasinensis* petals present in Hibiscus tea is sufficient to elicit anti-hyperglycemic, anti-hyperlipidemic, anti-hypertensive, anti-inflammatory, anti-anxiety and anti-oxidant properties without causing acute toxicity.

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