The positive effects of motherwort (*Leonurus cardiaca*) plant in improving heart health and reducing heart attacks and strokes in laboratory rats

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Abstract

Heart attacks and strokes have a few things in common: both are medical emergencies caused by a sudden interruption in blood flow. In a heart attack, the blood supply to your heart is suddenly interrupted. A stroke is caused by a sudden interruption of blood flow to your brain. For both conditions, timely medical care is crucial to reduce damage to the brain or heart. Therefore, the aim of this study was to determine the beneficial effects of motherwort (Leonurus cardiaca) on improving heart health and reducing heart attacks and strokes in laboratory rats. Twenty-four (24) male albino rats of the Sprague-Dawley strain weighing 150 ± 10 g at ten weeks of age were divided into four groups, one of which served as a negative control (normal) and the other groups were treated with adriamycin (ADM) by intraperitoneal injection (5 mg/kg) twice a week for a period of two weeks to induce heart disorder . One of the heart diseases is a positive control fed with a standard diet, and two of them were fed with (10% and 15%) motherwort (Leonurus cardiaca) for 28 days. At the end of the experiment, a blood sample was taken and the organs were harvested and subjected to biochemical analysis. The result showed thatthe rats in group 3 and had a significant increase in total cholesterol, triglycerides, high density lipoproteins-cholesterol, low density lipoproteins-cholesterol and very low density lipoproteins-cholesterol in blood serum, in contrast to HDL, which showed a significant decrease compared to the negative control (P<0.05). The study suggests using motherwort at 5% and 10%doses in the diet to lower LDL levels and atherogenicity index.

Key words: *Motherwort, heart attacks, strokes, heart disorder.*

1- INTRODUCTION

Interest in phytotherapy and the use of herbal medicines in the complex treatment of numerous clinical categories has been revived in modern times. In this day and age of synthetic medicines, there is a demand for herbal therapies that are tolerated by people, have a low risk of side effects and can be used in a variety of ways without the need to use xenobiotics. With this in mind, one of the main focuses of research in the pharmaceutical industry is to expand the range of herbal raw material sources for herbal treatments, Grudzinskaya et al. (2014). Motherwort is a traditional remedy that has been used for centuries. About two thousand years ago, the Tibetan people began using the motherwort plant for therapeutic purposes , Danilov et al. (2011). It was employed as a sedative and treatment for respiratory and cardiovascular illness in the Middle Ages. Universities, monasteries, and even people's homes grew the plant in their windows. The earliest recorded usage of motherwort to alleviate symptoms of coughing and palpitations in Russia was in the year 1485, Rauwald et al. (2013). The motherwort genus, also known as Leonurus L., belongs to the Lamiaceae family, also known as Lamiaceae Lindl. One of the two species of motherwort, motherwort cardiaca, is included in the pharmacopoeia of the USSR State. Motherwort is considered an officinal medicinal herb and five-lobed motherwort (Leonurus quinquelobatus Gilib.) are both medicinal plants that have a significant history of use in scientific medicine and are listed in the bulk of the pharmacopoeias that are written around the world. Barnes et al. (2002).

In addition to volatile oils, tannins, sterols, phenolic acids, Leonurus cardiaca consists of nitrogen-containing chemicals, phenylpropanoids, flavonoids, and phenolic acids. A minimum of 0.2 percent flavonoid content, often standardized to hyperoside content, is recommended for Leonurus supplements. Leonurus also includes the iridoid glycoside leonuride, as well as the leonurinine, alkaloids leonurine, stachydrine, all of which have been attributed to therapeutic properties Hardy et al. (2017). Agents that maintain mitochondrial activity display promise in stabilizing heart function and guarding against cardiovascular disease, which is important since heart attacks sometimes entail a change of mitochondria in cardiac muscle. Chlorogenic acid, quercetin, orientin, hyperoside and rutin are all components of Leonurus that are said to have an antioxidant effect and have been shown to reduce the formation of reactive oxygen species in the mitochondria . This has been hypothesized as a method of cardioprotection. Motherwort may preserve heart muscle mitochondria in a way that protects cell viability, because oxidative stress is known to promote death of functional cardiomyocytes. Kim et al. (2016). Motherwort has been used for thousands of years as a galactogenic and uterus-strengthening agent in prenatal and postnatal care. Due to its emmenagogue properties, likely due to both hormonal and vascular effects, it has been used to treat a variety of gynaecological and obstetrical problems such as amenorrhea, fertility, menstrual cramps and thyroid abnormalities. Anti-cancer studies have focused on feverfew's potential to reduce the growth of breast cancer cells and uterine fibroids according to Daiber et al. (2017). There is no evidence that Leonurus is poisonous or has any negative side effects, Gao et al. (2015). Strokes and heart attacks have many things in common: Both result from a rapid decrease in blood flow and are therefore considered medical emergencies. In a heart attack, the heart suffers from a sudden interruption of the blood supply. If the blood supply to the brain is suddenly interrupted, this can lead to a stroke. In all cases, it is important to see a doctor quickly to avoid the risk of permanent damage to the brain or heart Nakamura et al. (2013). Clinical investigations have indicated that Leonurus cardiaca possesses antioxidant and anti-inflammatory activity and can enhance heart function and blood circulation . One small pilot research looked at the effects of a daily dosage of 1200 mg of Leonurus on people with hypertension, anxiety, and sleep problems. After 4 weeks, there was a noticeable improvement in patients' mental and emotional wellbeing and blood pressure without any serious adverse effects as reported by Cheng et al. (2020).

2) AIM OF STUDY

The purpose of the trail was to investigate the protective advantages of the motherwort (Leonurus cardiaca) plant against cardiovascular disease in experimental rats.

3- MATERIALS & METHODS

3.1- Materials

3.1.1 preparation of motherwort (Leonurus cardiaca):

Motherwort (*Leonurus cardiaca*) was acquired at the Jeddah KSA market, washed, dried in 50 °C oven for three days, crushed & processed into fine powder.

3.1.2 Adriamycin injectable solution:

An intravenous solution of adriamycin (25 mg/ml) was obtained from Mina pharm Co., Cairo, Egypt. The El-Gomhoreya Company in Cairo, Egypt provided all additional chemicals, kits, or reagents.

3.2- Methods

3.2.1- Biological experiment

3.2.1.1- Basal diet composition of rats

The basil diet contained 10% casein, 0.25% choline chloride, vitamin mixture (1%), 5% cellulose, 10% maize oil, 4% salt mixture, 0.35% methionine, and corn starch (69.5%) (Morsi, 1992). The basal diet in the test contained CaCO3 (600 mg), $MgSO_4.2H_2O$ (204 mg), K_2HPO_4 (645 mg), $CaHPO_4.2H_2O$(150 mg), $Fe(C_6H_5O_7)_26H_2O$ (55 mg), $ZnCl_2$ (0.5 mg), $MnSO_4.4H_2O$ (10 mg), NaCl(334 mg), $CuSO_4.5H_2O$ (0.06 mg) and Kl (1.6 mg), (Hegsted et al. 1941). The basal diet in the test contained Vitamin A (200 Iu), Vitamin K (0.50 Iu), Vitamin E (10 Iu), Calcium panthothenic acid (0.40 mg), Thiamin (0.50 mg), Pyridoxine (1.00mg), Vitamin D (100 Iu), Folic acid (0.02 mg), Niacin (4.00 mg), Para-amino – benzoic acid (0.02 mg), Choline chloride (200 mg), Inositol (24 mg), Vitamin B12 (2.00 g) (Campbell, 1963).

Table 1. Shows the basic & experimental intakes' compositions.

Component (g)	Basal diet	10% Hawthorn	15% Hawthorn
Test ingredients	---	10	15
Casein	20	20	20
Corn oil	4.7	4.7	4.7
Mineral mix	3.5	3.5	3.5
Vitamin mix	1	1	1
Cellulose	5	5	5
Cholin chloride	2	2	2
Sucrose	10	10	10
Corn starch	Up to 100	Up to 100	Up to 100

3.2.2 Induction of disorder heart

Heart disorder groups were treated with adriamycin (ADM) for two days a week by intraperitoneal injection (5 mg/kg) twice a week for a total of two wk, to induce CVD according to Young et al. (2002).

3.2.3 Experimental Design & Animal Groups:

3.1.2- Experimental animals:

Twenty-four (24) Sprague Dawley male albino rats (with an average weight of 150±10g) at ten weeks old were utilized. The animals were kept in plastic cages that were free of metal components, and they were exposed to thorough cleanliness protocols. Before commencing the trial, rats were adapted to the baseline diet for 7 days. To prevent waste in addition to contamination, rats were nourished from special non-scattering feeding cups. Free water was available at all times from a bottle with a tiny opening and a metal tube securely fastened to the top of the bottle with rubber tubing.

As mentioned previously, in order to acclimate the animals for the experiment, they were housed on a 12/12 schedule for 7 days before the commencement of the trial. The rats were separated into 4 collections:

- Group 1: 6 rats were fed a baseline diet (control -ve).
- Group 2: 6 heart disease rats fed a baseline diet (control +ve).
- Group 3: 6 rats with heart disease received a 10% motherwort baseline diet.
- Group 4: 6 heart disease rats were administered a basic diet with 15% motherwort.

3.2.4 Biological evaluation

Daily feed consumption was documented, while body weight was assessed on a weekly basis for the duration of the 28-day experiment. In accordance with (Chapman et al., 1959), we calculated the body weight gain% (B.W. G.%), the food efficiency ratio & the weight of various organs.

3.2.4.1 Blood sampling

After twenty-eight days of testing, the rats were anesthetized with ether before being placed under anesthesia. Blood samples were collected in a dry centrifuge tube using a retro-orbital technique. After clotting for twenty minutes at room temperature, they were centrifuged at 1500 rpm for 1/4 hour. After the serum was collected with a sterile syringe, the samples were transferred to Wisserman tubes and stored at -10 °C until biochemical analysis could be performed. According to the procedures in (Drury and Wallington, 1967), rats were dissected open, their organs removed, rinsed in a saline solution and then dried after that weighed.

3.2.5 Biochemical analysis

3.2.5.1. Determination of lipids present in serum:

- Determination of triglycerides (TG): were calculated utilizing an enzyme calorimeter as described by Fassati & Prencipe (1982).
- Determination of total cholesterol (TC): The primary usage of TC testing, as stated by Allain, (1974).
- Determination of high-density lipoprotein cholesterol (HDL-c): The same procedure utilized for evaluating total cholesterol may be used for determining the HDL fraction of cholesterol contained in a supernatant precipitated with phosphotungstic acid & magnesium ions, consistent with Lopez, (1977).
- Determination of very low-density lipoprotein cholesterol (VLDL-c): have been assessed by Lee and Nieman's (1996) methodology.
- Determination of low-density lipoprotein cholesterol (LDL-c): Serum low-density lipoprotein cholesterol was calculated the equation by Castelli et al. (1977).
- Total Lipids: The amount of lipids was measured by a colorimetric assay. (In accordance with schmit 1964)

3.2.5.2. liver functions Determination

- Determination of Alanine transferase (ALT): The technique of Tietz (1976) was used to calculate ALT. L-alanine is converted to pyruvate and glutamate by ALT, an enzyme that causes a reaction to occur an amino transfer from L-alanine to a-ketoglutarate.
- Aspartate transferase (AST) Determination: The measurement Aspartate transferase of was done consistent with the technique of Henry (1974) and Yound (1975).

3.2.5.3. Determination of e Kidney functions

- Determination of Creatinine: Creatinine was estimated utilizing Henry (1974) kinetic procedure.
- Determination of urea: Urea was identified via Patton and Crouch's (1977) enzymatic technique.

3.2.5.4 Serum anti-oxidation enzyme activity:

The approach of (Paglia and Valentine, 1967) was employed to measure the GPX enzyme activity. The method of (Aebi, 1984) was used to measure the activity of the antioxidant enzyme MID.

3.2.6 Statistical Analysis:

One-way classification was employed for the statistical analysis. Least significant distinction (LSD) & analysis of variance (ANOVA) in accordance with (Snedcor and Cochran, 1967). the values are expressed in mean ± SD with a group of letters like (a-b-c-d etc.) Mean value with different letters in the same column are significantly different ($P<0.05$). As the difference of letters indicates the existence of statistical differences, and when the letters are similar, it indicates that the groups are similar in their effects.

4) RESULTS & DISCUSSION

This research intended to know the positive effects of motherwort (*Leonurus cardiaca*) plant in improving heart health and reducing heart attacks and strokes in laboratory rats.

4.1. Biological results

4.1.1. Effect Of different levels of Motherwort (Leonurus cardiaca)On Lipids Profile And Atherogenic in Index Negative Control And Adriamycine Groups.

The effect of motherwort (Leonurus cardiaca) on of lipids profile of negative control and adriamycine groups are shown in table (2 and 3). Exposing rats to ADM led to a significant increase in the levels of TC, TG, LDL, VLDL and atherogenic index in the blood serum, in contrast to HDL which showed a significant decrease compared with the negative control (P< 0.05). The negative control group shows a superior lipid profile relative to the adriamycin group when compared with the negative control (P< 0.05). The same results were obtained by Kim et al. (2016), heart attacks are often associated with changes in the mitochondria of the heart muscle, and agents that support mitochondrial function show promise for maintaining heart function and protecting against cardiovascular disease. The Leonurus constituents chlorogenic acid, orientin, quercetin, hyperoside and rutin are said to have an antioxidant effect. They have been shown to reduce the production of reactive oxygen species in the mitochondria - a proposed mechanism for protecting the heart. Oxidative stress also induces apoptosis of functioning cardiomyocytes, and feverfew may protect the mitochondria of the heart muscle.

Nakamura et al. (2011). Leonurus cardiaca has been credited with antioxidant and antiinflammatory activity and an ability to improve heart function and blood circulation, partly via mild negative chronotropic effects and hypotensive activity, as has been demonstrated in clinical trials. One human pilot study investigated Leonurus dosed at 1200 mg/day in patients with hypertension accompanied by anxiety and sleep disorders. A positive effect on mental emotional status and hypertension was reported after 4 weeks, without significant side effects. Twenty-five according to the Clinical Global Impression Scale, a significant improvement in anxiety and depression parameters was observed in 32% of patients, a moderate improvement in 48% of patients and a weak effect in 8% of patients. Twelve percent of patients did not respond to the therapy. Cheng et al. (2020).

Table 2. Impact of Motherwort (Leonurus cardiaca) on of lipids profile negative control & adriamycine groups.

Variables Groups	Total cholesterol (mg/dl)	Triglycerides (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)
Negative control	$57.50^{c}\pm5.69$	$67.94^{c}\pm7.19$	$27.00^{a}\pm0.82$	$16.91\ ^{c}\pm4.08$	$13.59^{c}\pm1.44$
Positive Control	$239.00^{a}\pm6.48$	$187.50^{a}\pm11.90$	$23.75^{bcd}\pm1.71$	$77.75^{a}\pm8.54$	$37.50^{a}\pm2.80$
10% Motherwort	$110.\ ^{b}\pm8.04$	$65.00\ ^{c}\pm1.41$	$24.50\ ^{c}\pm1.29$	72.5b ±8.12	$13.00^{c}\pm.28$
15% Motherwort	$110.5^{b}\pm8.35$	$69.25^{c}\pm4.50$	$22.25^{d}\pm1.71$	74.4b ±9.54	$13.85^{c}\pm0.9$

All results are expressed as mean ± SD (standard deviation of the mean).
* Values in each column with different letters are significantly different (P < 0.05).
* One way ANOVA test was used.

Table 3. Influence of Motherwort (Leonurus cardiaca) on atherogenic index negative control as well as adriamycine groups.

Variables Groups	AC (mg/dl)	CRR (mg/dl)	Al (mg/dl)
Negative control	$1.29^{d}\pm0.18$	$2.13^{d}\pm0.18$	$0.40^{ef}\pm0.05$
Positive Control	$9.10^{a}\pm0.75$	$10.10^{a}\pm0.75$	$0.90^{a}\pm0.05$
10% Motherwort	$3.50^{c}\pm0.37$	$4.50^{c}\pm0.37$	$0.42^{e}\pm0.03$
15% Motherwort	$4.01^{b}\pm0.74$	$5.01^{b}\pm0.74$	$0.49^{d}\pm0.05$

All results are expressed as mean ± SD (standard deviation of the mean).
* Values in each column with different letters are significantly different (P < 0.05).
* One way ANOVA test was used.

4.1.2. Effect of Motherwort (Leonurus cardiaca) on Liver Functions of Negative Control also Adriamycine Groups.

The effect of motherwort (Leonurus cardiaca) on liver functions of negative control and adriamycine groups are shown in Table (4), Exposure rats to ADM led to a significant increase in the levels of ALT and AST in the blood serum compared with the negative control (P< 0.05). The same results were obtained by Lee et al . (2017). reported that saponins in herbs have hepatoprotective effects, so we can say that motherwort has hepatoprotective effects.

Table 4. Effect of Motherwort (*Leonurus cardiaca*) on liver functions of negative control and adriamycine groups.

Variables Groups	ALT(U/L)	AST(U/L)
Negative control	$35.00^{e}\pm2.16$	$30.00^{e}\pm4.00$
Positive Control	$60.25^{a}\pm6.85$	$56.75^{ab}\pm5.68$
10% Motherwort	$54.00^{ab}\pm7.35$	49.50 ± 1.25
15% Motherwort	$39.00^{de}\pm7.12$	$51.00^{bcd}\pm4.08$

All results are expressed as mean ± SD (standard deviation of the mean).
* Values in each column with different letters are significantly different (P < 0.05).
* One way ANOVA test was used.

4.1.3. Effect of Motherwort (Leonurus cardiaca) on kidney functions of negative control & adriamycine groups

Table (5) showed the effect of Motherwort (*Leonurus cardiaca*) on kidney functions of negative control & adriamycine collections. Exposure rats to ADM led to a substantial rise in the levels of creatinine & urea in the serum (P< 0.05). Feeding rats on diet replaced with different concentration resulting in significant reduction the level of creatinine & urea serum. . The same results were obtained by Leite et al . (2016). designated that Leonurus cardiaca powder treatment decreases the likelihood of subcapsular fibrosis as well as microcalcifications in the kidneys, as well as the generation of calcium oxalate crystals. The levels of serum urea and creatinine were significantly reduced by sambucus, and this effect was dose-dependent.

Table (5): Impact of Motherwort (*Leonurus cardiaca*) on kidney functions of -ve control & adriamycine groups

Variables Groups	Creatinine(mg/dl)	Urea(mg/dl)
Negative control	$0.87^{c}\pm0.04$	$6.94^{h}\pm0.83$
Positive Control	$1.78^{a}\pm0.09$	$27.00^{a}\pm1.41$
10% Motherwort	$0.83^{cd}\pm0.08$	$14.25^{f}\pm1.26$
15% Motherwort	$0.83^{cd}\pm0.08$	$14.25^{f}\pm1.26$

All results are expressed as mean ± SD (standard deviation of the mean).
* Values in each column with different letters are significantly different ($P < 0.05$).
* One way ANOVA test was used.

4.1.4. Effect of Motherwort (Leonurus cardiaca) on Antioxidant Activity of Negative Control and Adriamycine Groups

The effect of an antioxidant activity of negative control & adriamycine collections are revealed in table (6), Exposure rats to ADM led to a substantial increase in the levels of MDA & GPx contrasted with the -ve control. The same results were obtained by Kuhn et al. (2020). Motherwort plant which is rich in antioxidants, this could be beneficial in increasing the levels of MID, GPX, as well as CAT. Also this results agree ment with Kuchta et al. (2023), motherwort extract is rich in flavonoids, terpenoids and other phenolic acids. These substances have a strong antioxidant effect. They destroy free radicals and harmful molecules that cause oxidative stress and damage cells. They help to protect your organs and prevent chronic or long-term diseases.

Table 6. Effect of Motherwort *(Leonurus cardiaca)* on antioxidant activity of negative control and adriamycine groups.

Variables Groups	MDA (nrol/mL)	GPx (mu/ml)
Negative control	15.62^{d}=fc 1.55	$5.22^{f}\pm1.55$
Positive Control	$38.90^{a}\pm4.23$	$15.94^{de}\pm1.28$
10% Motherwort	$35.28^{ab}\pm3.13$	19.29^0.57
15% Motherwort	$37.20^{a}\pm0.95$	19.36^1.72

All results are expressed as mean ± SD (standard deviation of the mean).
* Values in each column with different letters are significantly different ($P < 0.05$).
* One way ANOVA test was used.

5. Conclusion

Laboratory studies have confirmed the adaptogenic properties and benefits of motherwort (Leonurus cardiaca)This is because it contains many nutrients that can lower blood sugar and have a positive effect on weight, in addition to its good effect on blood lipids, liver enzymes and kidney function. The plant is mostly harmless. Only mild to severe adverse effects have been documented in experiments. Precautions must be taken when motherwort (*Leonurus cardiaca*) is administered together with some medicines and in the long term. Based on the results, it is important to increase the use of Motherwort (*Leonurus cardiaca*) in our daily lives is because of its benefits in improving many diseases such as cardiovascular diseases and thus strokes. Additionally, Motherwort (*Leonurus cardiaca*) (10%, 15%) has ability to improve lipid profiles. It is also important to carry out programs for nutritive education to explain the dangers of cardiovascular disease, nutritional recommendations for this disease, and increased consumption of Motherwort (*Leonurus cardiaca*).

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