Original Research

HEPATOCARDIOPROTECTIVE EFFECT OF *Brassica Oleracea* IN HALOFANTRINE INDUCED HEPATO-CARDIOTOXICITY IN RATS.

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ABSTRACT

The use of antimalarial drug halofantrine is associated with hepato-cardiotoxicity. The main objective of this study is to investigate the effect of aqueous extract of *Brassica oleracea* (Cabbage) on halofantrine induced liver and heart damage. Methodology included collection of *Brassica oleracea* and preparation of its extract, oral administration of the sample materials (halofantrine/vegetable) into the experimental wistar albino rats as well as biochemical evaluation of serum liver enzymes; {Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), Alkaline phosphatase (ALP)}, heart marker enzymes ;{ Creatine kinase (CK) and Lactate dehydrogenase (LDH)} and concentration of Malondialdehyde (MDA) after 16, 96 and 192 hours. The result showed that the groups administered with halofantrine alone had significant increase ($p<0.05$) in the activities of all the enzymes with a peak at the 16th hour compared with the normal control. Malondialdehyde had a peak at the 192 hour. Coadministration of aqueous *Brassica oleracea* resulted in significant decreases ($p<0.05$) in the enzyme activities and concentration of malondialdehyde as compared with those recorded from administration of halofantrine alone. Results of this study suggest that *Brassica oleracea* aqueous extract can provide hepatocardio protective effect against halofantrine induced hepatocardio toxicity.

Keywords: Halofantrine, *Brassica oleracea,* Hepatocardiotoxicity, malondialdehyde, Liver enzymes.

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INTRODUCTION:

Halofantrine, a lipophilic phenanthrene methanol belonging to the aryl amino alcohol is used for the treatment of acute uncomplicated multi-drug resistant malaria[12]. It is schizonticidal with high degrees of activity against the asexual erythrocytic stage of malarial infections caused by single or mixed infections of *Plasmodium falciparium* or *Plasmodium vivax*. It has limited effect against the exoerythrocytic or gametocyte stages of malaria parasites[15]. Clinical treatment with halofantrine is often accompanied by serious side effects such as abdominal pain, diarrhoea, vomiting, rash, headache, and itching, elevated liver enzymes, prolongation of QTc interval and arrhythmias that could be fatal. However, an increasing number of reports describing serious complications in the last few years have raised some doubt about the safety of halofantrine[16]. Halofantrine has been reported to be cardiotoxic[10, 16]. Also several studies have shown that other antimalarials such as chloroquine and quinine are hepatoxic[11, 3]. Halofantrine is marketed as Halfan and is never used to prevent malaria. A crystallographic study has shown that halofantrine binds to hematin *in vitro*, suggesting a possible mechanism of action. Alternatively or in addition, halofantrine has been shown to bind to plasmepsin, a hemoglobin degrading enzyme unique to the malarial parasites. It appears to inhibit polymerization of heme molecules (by the parasite enzyme "heme polymerase"), resulting in the parasite being poisoned by its own waste (by forming toxic complexes with ferritoporphyrin IX that damage the membrane of the parasite.). Halofantrine has been shown to preferentially block open and inactivated HERG channels leading to some degree of Cardiotoxicity. The absorption of halofantrine is erratic, but is increased when taken with fatty food. Because of fears of toxicity due to increased halofantrine blood levels, halofantrine should be taken on an empty stomach. Plasma levels peak at 16 hours and the half-life of the drug is about 4 days.

Brassica oleracea (cabbage) is of the family *Brassicaceae* (or *Cruciferae*) and is used as a leafy green vegetable. Cabbage can provide some special cholesterol-lowering benefits if cooked by steaming[18]. Cabbage can be used to provide cardiovascular system with valuable support in the form of cholesterol reduction[18]. In fact, when the cholesterol-lowering ability of steamed cabbage was compared with the cholesterol-lowering ability of the prescription drug cholestyramine (a medication that is taken for the purpose of lowering cholesterol), cabbage bound 17% as many bile acids (based on a standard of comparison involving total dietary fiber)[18].

Researchers now realize that different types of cabbage (red, green, and Savoy) contain different patterns of glucosinolates. Cabbage in general—but also Savoy cabbage in particular—turns out to be an especially good source of sinigrin. Sinigrin is one of the cabbage glucosinolates that has received special attention in cancer prevention research. The sinigrin in cabbage can be converted into allyl-isothiocyanate, or AITC, a compound that has unique cancer preventive properties with respect to bladder cancer, colon cancer, and prostate cancer[18]. The isothiocyanate (ITCs) made from cabbage's glucosinolates act to protect against cancer through a variety of different mechanisms. In some cases, they help regulate inflammation by altering the activity of messaging molecules within the body's inflammatory system. In other cases, they improve the body's detoxification system and leave the cells with a smaller toxic load. But the bottom line is decreased risk of cancer from consumption of cabbage and its glucosinolates cancer[18]. The uniqueness of cabbage in cancer prevention is due to the three different types of nutrient richness found in this widely enjoyed food. The three types are (1) antioxidant richness, (2) anti-inflammatory richness, and (3) richness in glucosinolates[18].

Long-established in health research is the role of cabbage juice in helping heal stomach ulcers (called peptic ulcers), but more recent studies on cabbage have looked at the overall health benefits of this food for the stomach and digestive tract as a whole cancer[18]. Present-day studies make it clear that cabbage contains a variety of nutrients of potential benefit to our stomach and intestinal linings. These nutrients include glucosinolates (and the anti-inflammatory isothiocyanate or ITCs made from them), antioxidant Polyphenols, and the amino acid-like substance called glutamine. In the case of ITCs, digestive tract benefits include proper regulation of bacterial populations of Helicobacter pylori inside the stomach[18].

Cabbage ranked in WHFoods rating system as an excellent source of vitamin C and a good source of vitamin A (which comes from its concentration of carotenoids such as beta-carotene). Cabbage is an excellent source of vitamins K and C. Where citrus fruits are not available or cannot be consumed due to health reasons, it is possible to supplement vitamin C naturally by drinking the raw cabbage juice. It is also a very good source of fiber, manganese, and folate. Cabbage is also a good source of molybdenum, vitamin B6, potassium, thiamin (vitamin B1), and calcium (the outside hard leaves of the cabbage are at least forty percent higher in calcium content, than the leaves found within the cabbage head)[18]. Cabbage is a good source of Vitamins B2, amino acids, and fats. Along with other Cole crops, cabbage is a source of indole-3-carbinol, a chemical that boosts DNA

repair in cells and appears to block the growth of cancer cells[6, 21]. Though it has a very low caloric value, the cabbage is very high in useful roughage and cellulose; it also gives an alkaline chemical reaction in the laboratory. The cabbage also contains high amounts of chlorine. It has good amounts of the mineral iodine - essential for the thyroid gland. It has high levels of the essential mineral phosphorus. Cabbage also has important metabolic salts such as the mineral sodium, and is sulfur rich vegetable. Cabbage is not a fatty food! But among the little bit of fat it contains, there is a surprising amount of one particular omega-3 fatty acid called alpha-linolenic acid, or ALA[18].

Polyphenols ranked high on the list for phytonutrient antioxidants in cabbage. In fact, one group of researchers has described Polyphenols as the primary factor in cabbage's overall antioxidant capacity. The antioxidant richness of cabbage is partly responsible for its cancer prevention benefits. Without sufficient intake of antioxidants, oxygen metabolism can become compromised, and a metabolic problem called oxidative stress can be experienced. Chronic oxidative stress—in and of it—can be a risk factor for development of cancer[18].

Without sufficient intake of anti-inflammatory nutrients, regulation of inflammatory system can become compromised, and the problem of chronic inflammation can be experienced. Especially when combined together with oxidative stress, chronic inflammation is a risk factor for development of cancer[18]. The anthocyanins found in red cabbage are well-documented anti-inflammatory compounds, and make red cabbage a standout anti-inflammatory food for this reason. However, all types of cabbage contain significant amounts of Polyphenols that provide anti-inflammatory benefits[18].

In addition to its usual purpose as an edible vegetable, cabbage has been used historically as a medicinal herb. It has been recommended for drunkenness–both preventatively to prevent the effects of alcohol, and to cure hangovers[3]. In Cato the Elder's work *De Agri Cultura* ("On Agriculture"), he suggested that women could prevent diseases in their private parts by bathing in urine obtained from those who had frequently eaten cabbage[19]. The cooling properties of the leaves were used in Britain as compresses for ulcers and breast abscesses, and as a treatment for trench foot in World War I. Other medicinal uses recorded in Europe folk medicine include treatments for rheumatism, sore throat, hoarseness, colic, and melancholy[3].

In the United States, cabbage has been used as a hangover cure, to treat abscesses, to prevent sunstroke, or to cool body parts affected by fevers. The leaves have also been used to sooth sore feet, and, tied around the neck of children, to relieve croup. Mashed cabbage and cabbage juice have been used in poultices to remove boils and treat warts, pneumonia, appendicitis, and ulcers[8].

The herbal poultice for the treatment of external injuries is the best known of all cabbage derived herbal medications. The detoxification effect of the cabbage is significant, at the same time, the vegetable is considered very helpful in the treatment of painful arthritis over the long term. The vitamin C deficiency disease called scurvy can be beaten back and cured by eating raw cabbage rich in vitamin C[18].

Packed cabbage leaves were often used as topical eczema remedies in many parts of Europe in earlier times. The cabbage was also used for the treatment of different disorders affecting the legs - including the varicose veins and in the alleviation of leg ulcers of all sorts. When used as internal as well as external remedy, cabbage is useful mainly due to its high sulfur content, the mineral destroys the ferments within the blood, and this is particularly effective as a treatment for skin disorders of all kinds. Individuals affected by persistent coldness in the feet can benefit by including cabbage in the daily diet, this is because sulfur is considered to be one of those elements that can induce an increase in the production of heat in the body. Disorders like constipation and diabetes can be treated using the cabbage. Other medicinal uses include Pancreatic cancer, Prostate cancer, Stomach cancer and Toxic shock syndrome[18].

The leaves of the cabbage can be used to prepare an herbal decoction for the treatment of disorders such as colitis. Leaves of the cabbage can also be turned into a combination of herbal lotion with witch hazel, for the treatment of skin disorders such as the common acne. The juice of the cabbage is used for the treatment of ulcers that are intestinal in origin or specifically those which affect the duodenum. Many herbalists will often suggest this juice as an initial treatment for many patients suffering from gastric ulcers. The leaves of the cabbage can be prepared into herbal syrup; this is made from the cabbage decoction. Dosage of the syrup can be 10 ml daily, for the treatment of hacking and persistent coughs, the syrup is also useful in the treatment of the asthma symptoms, and as a remedy for bronchitis which is persistent or symptomatically severe[18].

STUDY OBJECTIVES

The main objective of the present study is to investigate the therapeutic potential of *Brassica oleracea* in offering protection against hepatocardiotoxicity effect of halofantrine through assessment of liver and heart marker enzymes and Malondialdehyde.

STUDY HYPOTHESIS

There are existing literature pointing that halofantrine can cause hepato- and cardiotoxicty. According to this context, it is hypothesized that *Brassica oleracea*, a vegetable commonly consumed by the people, will offer hepatocardio protection compared with the halofantrine induced hepatocardiotoxic group.

METHODOLOGY

Methodology included collection of *Brassica oleracea* and preparation of its extracts, induction of hepatocardiotoxicity and biochemical evaluation of liver and heart marker enzymes and Malondialdehyde.

Collection of *Brassica oleracea* and preparation of its extraction

Brassica oleracea was bought from Sharada Market, Municipal Local Government, Kano State. The leaves were cleaned of dirt and blot, weighed and blended using an electric blender. The paste was filtered using cheesecloth and the filtrate evaporated by the use of Rotary evaporator and reweighed. The difference between the weight of extract and the initial weight of the vegetables gives the concentration of the extract.

Collection of Halofantrine tablet

Halofantrine tablet (Halfan, GlaxoSmithKline group of companies) was obtained from a registered pharmaceutical store at Kofar Nassarawa, Kano Municipal Council, Nigeria, and was used before expiry date.

Animals

Wistar albino rats of both sexes were obtained from university of Jos, Plateau State and kept in the animal house of Biological Sciences Department, Bayero University Kano, Nigeria. The rats were kept under the same atmospheric conditions for about two weeks to acclimatize, and had free access to normal diet (Growth marsh, Vital feeds Ltd) and water.

Forty five (45) wistar albino rats weighing 100-120 grams were divided into five (5) groups of nine (9) rats each. Rats in group I served as the normal control. For groups II-IV, the effect of halofantrine on some liver and heart enzymes were determined by administering 7.10, 14.20 and 21.30mg/kg of halofantrine drug respectively. Group V was orally co-administered with halofantrine and cabbage extract; 7.10 and 0.10mg/Kg respectively.

Three rats were removed from each group after 16, 96 and 192 hours of administration and sacrificed by decapitation, and blood serum kept for biochemical analysis. Serum was separated and analyzed for alanine aminotransferase(ALT) and aspartate aminotransferase (AST) activities by the method of Reitman and Frankel (1957)[14], serum alkaline phosphatase (ALP) activity by the method of Rec (1972)[13], serum lactate dehydrogenase by the spectrophotometric (kinetic) method of Wroblewski and La Due (1955)[20] as reported by Derek A. Woodrow (1987)[4],serum Creatine kinase by the colorimetrical method of Ennor and Rosenberg (1954)[5] as reported by Derek (1987)[4] and serum malondialdehyde (MDA)by the methods of Hunter *et al*.,(1963)[9], modified by Guttridge and Wilkins (1982)[7].

Statistical Analysis

Data is presented as mean ± standard deviation of 3 replicates. The significance difference between the means was assessed by one-way ANOVA. The level of significance was set at $P<0.05$.

RESULTS AND DISCUSSION

Results of the effect of halofantrine on the levels of some serum hepato-cardio toxicity enzyme indices in rats at 16, 96 and 192 hours are shown in Tables 1, 2 and 3. The tables showed the serum activities of liver maker enzymes (ALT, AST, and ALP),heart marker enzymes(LDH and CK) and concentration of Malondialdehyde (MDA) for groups (II-IV) of rats administered with 7.1, 14.2 and 21.3mg/kg Halofantrine after 16hrs, 96hrs and 192hrs respectively, and a control group I which was not treated with Halofantrine. There is significant difference ($p<0.05$) in all the parameters between group I and the test groups (II, III and IV) 16 hours after oral administration of Halofantrine. This may be due to leakage of the biochemical markers in the serum. The result showed no significant difference ($p>0.05$) in AST between groups I and II, I and III, as well as groups II and III, 96 hours after halofantrine administration. However, at 192 hours all the indices showed significant difference ($p<0.05$) among the groups. This may also be due to leakage of the biochemical markers in the serum.

Generally, measurement of Alanine transaminase (ALT), Aspartate transaminase (AST), and Alkaline phosphatase (ALP) are commonly used as marker enzymes of hepatotoxicity, while Malondialdehyde (MDA) is estimated as a marker for oxidative stress. The indices commonly used in Cardiotoxicity include; Lactate dehydrogenase (LDH) and Creatine kinase (CK) activities. Very high values of ALT are seen in acute hepatitis, either toxic or viral in origin. Both ALT and AST levels are increased in liver diseases, but ALT >> AST[17]. This information has been substantial and supported by the findings in tables 1, 2 and 3. Moderate increase in ALP level is seen in hepatic diseases such as infective hepatitis, alcoholic hepatitis or hepatocellular carcinoma. Very high activity of serum ALP than normal may be noticed in extrahepatic obstruction or cholestasis. This observation also agrees with the result of this study (Tables 1, 2 and 3). ALP is also produced by epithelial cells of biliary canaliculi and obstruction of bile with consequent irritation of

epithelial cells leads to secretion of ALP into serum. Detection of higher levels of MDA in the serum of Halofantrine treated rats than in control rats confirms that Halofantrine induces liver damage[1], and the level of the MDA generated increased with increase in halofantrine dosage as indicated in Tables 1, 2, and 3.This signifies that the degree of lipid peroxidation and liver damage increased with increase in the dose of halofantrine.

The rats orally administered with 7.1mg/Kg, 14.2mg/Kg and 21.3mg/Kg in 16, 96 and 192 hours had mean serum ALT, AST, ALP, CK and MDA significantly higher ($p<0.05$) than those in control rats (Tables 1, 2 and 3), except for AST in group IV (Table 1), and LDH. This therefore, supports the statement that Halofantrine administration even under therapeutic dose can cause increase in serum liver and heart enzymes. The serum ALT activities in rats treated with normal dose of Halofantrine increased after 16, 96 and 192 hours. This shows that the effect of halofantrine as hepato toxin is increasing with increase in time. The rats treated with triple normal dose (21.3mg/Kg) of halofantrine showed decrease in serum ALP concentration (but higher than that in the control rats). This could be due to natural healing that possibly occurred with time after 21.3mg/Kg halofantrine administration and it confirms the fact that liver cells are capable of regenerating naturally, especially when the toxic agent is eliminated. The serum ALT, AST, ALP, CK and LDH activities are significantly higher than those in control rats with moderate increase in rats treated with twice normal dose (14.2mg/Kg) of halofantrine drug. This could also be due to the natural healing. Overall, administration of halofantrine (even at various doses) gives rise to an ideal hepato, cardiotoxic ability of the drug.

Group V was treated with 7.1mg/Kg halofantrine and 0.1mg/Kg cabbage extract. The levels of AST, ALP, CK and LDH in the group showed significant difference ($P<0.05$) 16 hours after administration of extract(s). There was no significant difference in ALT ($P>0.05$) between groups I and V at 16hrs after extract administration. Similarly, the levels of MDA in groups I and V showed no significant difference ($P>0.05$) 16 hours after oral extract administration. The results of oral administration of the vegetable extract after 96 and 192 hours revealed significant difference ($P<0.05$) in all the parameters. This shows possible hepatocytes preventive effect of the vegetable against halofantrine toxicity.

The possible hepato and cardio protective effects of the vegetable could be attributed to its chemical constituents that have antioxidants and/or coenzyme property. Cabbage (*Brassica oleracea*) is an excellent source of vitamins C and K, and a good source of vitamin A. It provides calcium, potassium, chlorine, iodine, phosphorous, sodium, sulphur and phytonutrient polyphenol that all act as antioxidants and/or coenzymes. Cabbage is a source of indole-3-carbinol, a chemical that boost DNA repair in cells and appears to block the growth of cancer cells[6, 21].

Table 1: Serum ALT, AST, ALP, CK and LDH activities and MDA levels in rats 16 hours after oral administration of Halofantrine drug.

Group/treatment	ALT(U/L)	AST(U/L)	ALP(U/L)	CK(U/L)	LDH(U/L)	MDA(μM)
Group I (No Halofantrine)	43.00^{a} ± 0.09	16.00^{b} ± 0.02	1001.51^{c} ± 0.25	90.79^{d} ± 0.02	17761.24^{e} ± 0.13	6.49^{f} ± 0.03
Group II (7.1 mg/kg Halofantrine)	52.00^{a} ± 0.09	23.00^{b} ± 0.02	5737.73^{c} ± 0.36	1905.30^{d} ± 0.37	14718.21^{e} ± 0.10	20.74^{f} ± 0.04
Group III (14.2 mg/kg Halofantrine)	62.00^{a} ± 0.04	19.00^{b} ± 0.03	5235.41^{c} ± 0.43	705.72^{d} ± 0.07	12073.26^{e} ± 0.05	27.99^{f} ± 0.04
Group IV(21.3 mg/kg Halofantrine)	94.00^{a} ± 0.02	13.00^{b} ± 0.02	4568.72^{c} ± 0.76	1109.48^{d} ± 0.28	15672.00^{e} ± 0.07	28.23^{f} ± 0.04

Results are mean ± Standard deviation, n=3 and values in same column bearing similar super script are significantly different at P<0.05

Table 2: Serum ALT, AST, ALP, CK and LDH activities and MDA levels in rats 96 hours after oral administration of Halofantrine drug.

Group/treatment	ALT(U/L)	AST(U/L)	ALP(U/L)	CK(U/L)	LDH(U/L)	MDA(µM)
Group I (No Halofantrine)	43.00[a] ± 0.09	16.00[b] ± 0.02	1001.51[e] ± 0.25	90.79[f] ± 0.02	17761.24[g] ± 0.13	6.49[h] ± 0.03
Group II (7.1 mg/kg Halofantrine)	67.00[a] ± 0.05	16.00[c] ± 0.02	3316.60[e] ± 0.48	1646.67[f] ± 0.36	11183.60[g] ± 0.14	35.14[h] ± 0.04
Group III (14.2 mg/kg Halofantrine)	77.00[a] ± 0.12	16.00[d] ±	4214.83[e] ± 0.68	1188.58[f] ± 0.16	11945.02[g] ± 0.13	40.26[h] ± 0.01
Group IV(21.3 mg/kg Halofantrine)	52.00[a] ± 0.09	13.00[b, c, d] ± 0.02	2314.72[e] ± 0.44	517.94[f] ± 0.01	14159.83[g] ± 0.12	57.46[h] ± 0.20

Results are mean ± Standard deviation, n=3 and values in same column bearing similar super script are significantly different at P<0.05

Table 3: Serum ALT, AST, ALP, CK and LDH activities and MDA levels in rats 192hours after oral administration of Halofantrine drug.

Group/treatment	ALT(U/L)	AST(U/L)	ALP(U/L)	CK(U/L)	LDH(U/L)	MDA(µM)
Group I (No Halofantrine)	43.00[a] ± 0.09	16.0[b] ± 0.02	1001.51[c] ± 0.25	90.79[d] ± 0.02	17761.24[e] ± 0.13	6.49[f] ± 0.03
Group II (7.1 mg/kg Halofantrine)	94.00[a] ± 0.09	19.00[b] ± 0.04	3450.00[c] ± 0.60	1272.49[d] ± 0.17	10721.40[e] ± 0.05	35.87[f] ± 0.10
Group III (14.2 mg/kg Halofantrine)	72.00[a] ± 0.08	13.00[b] ± 0.02	3946.80[c] ± 0.35	859.10[d] ± 0.17	10229.81[e] ± 0.10	48.09[f] ± 0.003
Group IV (21.3 mg/kg Halofantrine)	48.00[a] ± 0.00	23.00[b] ± 0.03	3281.64[c] ± 0.06	878.02[d] ± 0.09	10876.36[e] ± 0.03	74.27[f] ± 0.25

Results are mean ± Standard deviation, n=3 and values in same column bearing similar super script are significantly different at P<0.05

Table 4: Serum ALT, AST, ALP, CK and LDH activities and MDA levels in rats 16 hours after Oral Co administration of Halofantrine and Cabbage extract.

Group	ALT(U/L)	AST(U/L)	ALP(U/L)	CK(U/L)	LDH(U/L)`	MDA(µM)
Group I (Normal control)	43.00^{a} ± 0.09	16.00^{d} ± 0.02	1001.51^{f} ± 0.25	90.79^{h} ± 0.02	17761.24^{j} ± 0.13	6.49^{l} ± 0.03
Group II (Test control, 7.1 mg/Kg halofantrine)	*$94.00^{a,c}$* ± *0.09*	*$19.00^{d,e}$* ± 0.04	*$3450.00^{f,g}$* ± *0.60*	*$1272.49^{h,i}$* ± *0.17*	*$10721.40^{j,k}$* ± *0.05*	*$35.87^{l,n}$* ± *0.10*
Group V (7.1mg/Kg halofantrine + 0.10mg/Kg cabbage extract)	$43.00^{b,c}$ ± 0.14	$67.00^{d,e}$ ± 0.08	$1078.61^{f,g}$ ± 0.10	$235.24^{h,i}$ ± 0.07	$5346.01^{j,k}$ ± 0.00	$6.59^{m,n}$ ± 0.01

Results are mean ±Standard deviation, n=3 and values in same column bearing similar super script are significantly different at P<0.05

Table 5: Serum ALT, AST, ALP, CK and LDH activities and MDA levels in rats 96 hours after oral co administration of Halofantrine and Cabbage extract.

Group	ALT(U/L)	AST(U/L)	ALP(U/L)	CK(U/L)	LDH(U/L)	MDA(µM)
Group I (Normal control)	43.00^{a} ± 0.09	16.00^{c} ± 0.02	1001.51^{e} ± 0.25	90.79^{g} ± 0.02	17761.24^{i} ± 0.13	6.49^{k} ± 0.03
Group II (Test control, 7.1 mg/Kg halofantrine)	*$94.00^{a,b}$* ± *0.09*	*$19.00^{c,d}$* ± 0.04	*$3450.00^{e,f}$* ± *0.60*	*$1272.49^{g,h}$* ± *0.17*	*$10721.40^{i,j}$* ± *0.05*	*$35.87^{k,l}$* ± *0.10*
Group V (7.1mg/Kg halofantrine + 0.10mg/Kg cabbage extract)	$72.00^{a,b}$ ± 0.00	$89.00^{c,d}$ ± 0.01	$2117.20^{e,f}$ ± 0.69	$10.32^{g,h}$ ± 0.002	$9361.52^{i,j}$ ± 0.00	$7.12^{k,l}$ ± 0.01

Results are mean ± Standard deviation, n=3 and values in same column bearing similar super script are significantly different at P<0.05

Table 6: Serum ALT, AST, ALP, CK and LDH activities and MDA levels in rats 192 hours after oral administration of Halofantrine and Cabbage extract.

Group	ALT(U/L)	AST(U/L)	ALP(U/L)	CK(U/L)	LDH(U/L)	MDA(µM)
Group I (Normal control)	43.00^{a} ± 0.09	16.00^{c} ± 0.02	1001.51^{e} ± 0.25	$90.79^{g,}$ ± 0.02	17761.24^{i} ± 0.13	6.49^{k} ± 0.03

Group II (Test control, 7.1 mg/Kg halofantrine)	*94.00*[a,b] ± *0.09*	*19.00*[c,d] ± 0.04	*3450.00*[e,f] ± *0.60*	*1272.49*[g,h] ± *0.17*	*10721.40*[i,j] ± *0.05*	*35.87*[k,l] ± *0.10*
Group V (7.1mg/Kg halofantrine + 0.10mg/Kg cabbage extract)	72.00[a,b] ± 0.02	52.00[c,d] ± 0.01	2076.35[e,f] ± 0.36	895.56[g,h] ± 0.00	8960.77[i,j] ± 0.00	28.81[k,l] ± 0.19

Results are mean ± Standard deviation, n=3 and values in same column bearing similar super script are significantly different at P<0.05

CONCLUSION

Halofantrine was found to elevate both liver and cardiac enzymes even under normal therapeutic dose. Experimental animals (albino rats) showed increase in serum liver and cardiac enzymes after oral administration of normal (7.1mg/Kg), twice (14.2mg/Kg) and triple (21.3mg/Kg) doses of the drug, 16, 96 and 192 hours after. Cabbage showed remarkable protective effect in the hepato-cardio toxicity of halofantrine. The experimental animals treated concurrently with the drug and vegetable extract showed reduced side effect produced by halofantrine. Hence the vegetable has some medicinal roles which may be due to its antioxidant and coenzymes composition. Therefore the claim hepato and cardio preventive roles of the vegetable may have some scientific basis. In general the vegetable may have significant role other than the present day perception (culinary purpose) among the local communities. Hence the fear of being poisoned by using halofantrine may now be minimized.

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