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Determination of the Effects of *Eruca sativa* Oil, Sodium Carbonate, Lavender Oil and *Aloe vera* Oil on Lipid Profile and Breast Tumour Markers in Breast Cancer-induced Doxorubicin Treated Female Albino Rats

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Author's contribution

The sole author designed, analysed, interpreted and prepared the manuscript.

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ABSTRACT

Background: Lavender oil, *Eruca sativa* oil and *Aloe vera* oil contain different types of fatty acids in addition to minerals, vitamins and other compounds which have anti-tumour action and antioxidant properties also it has cure properties against many other diseases. Sodium carbonate is alkaline material that affecting tissue PH and somewhat affecting on breast cancer through changing PH of the tissue making the medium not appropriate for breast cancer induction.
Aim: Is studying the effect of *Eruca sativa* oil, Sodium carbonate, Lavender oil and *Aloe vera* oil on lipid profile, Tumor markers of breast cancer and thyroid hormones.
Materials and Methods: Six groups of animals, five rats in each were used for this experiment and divided into negative control, positive control, sodium carbonate group, *Eruca sativa* oil group, lavender oil group and *Aloe vera* oil group. We induced cancer in all rats by MCF7 breast cancer cell line except negative control. Then all groups (Except positive and negative controls) were intraperitoneally (i.p.) injected with 2 mg /rat of adryadox (adryamycin chemotherapy), the remaining

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three groups except sodium carbonate group are supplemented with 1 ml. of the oil. Then rats are sacrificed and blood is centrifuged to obtain serum and analysis of lipid profile and breast cancer tumour markers.

Results: *Eruca sativa* oil and *Aloe vera* decrease cholesterol and triglycerides, where *Eruca s.* oil, Lavender oil and *Aloe vera* oil increase HDL more than sodium carbonate, *Erucas.* oil, Lavender oil and *Aloe vera* oil decrease LDL. *Eruca s.* oil decrease VLDL, sodium carbonate decreases alpha-fetoprotein and Ca15-3.

Conclusion and Recommendation: Based on the findings of this study, we recommend the use of lavender oil, *Eruca sativa* oil, *Aloe vera* oil and sodium carbonate administered at low doses as a helper in cure chemotherapy in treatment of breast cancer because it has useful effect in decreasing tumor markers and lipids and improve heart properties.

Keywords: Breast cancer; doxorubicin; Eruca sativa oil; sodium carbonate; lavender oil; Aloe vera oil.

1. INTRODUCTION

Many solid tumours are acidic in the extracellular pH as a result of poor perfusion and glycolytic metabolism. Metastatic potential is enhanced by acidity. Systemic administration of an alkaline agent such as sodium carbonate can buffer tumor acidity [1].

Oil contents are high in the seeds, glucosinolate, Erucic acid and protein contents the structurally unique and the major Glucosinolate in leaves *Eruca sativa* was identified as 4-mercaptobutyl GLS [2]. *Eruca sativa* leaves have three new quercetin glycosides [3]. When phytochemical investigations were done on aqueous extract of *Eruca sativa* fresh leaves it shows the presence of nine natural flavonoid compounds [4]. *Eruca sativa* decrease blood sugar and can treat diabetes and its complications [5].

Aloe vera, also known as *Curacaeo aloe* or Barbados, has been used in traditional medicine for thousands of years to cure a variety of diseases. Cultivation of the plant is easy it is native to the northern parts of Africa and widely spread across the world. The latex which derived from the bundle sheath cells has strong laxative and purgative properties. Mediterranean civilizations, Egyptians and A Syrians in biological times used this plant. Different species of Aloe are still used in folk medicines of Asia and Africa [6].

Scientists have studied the efficacy of *Aloe vera* gel to treat burns, genital herpes and seborrheic dermatitis in addition to allergic reactions and found it has an effect [7].

1,8-cineole, B-ocimene, Camphor and 4,1-Terpiven, so the relative levels of these constituents are varying in different species. Lavender oil is obtained from the flowers of *lavandula angustifolia* through steam distillation it is composed mainly of linalyl acetate lavandulol, linalool, lavanulyl acetate, 1, 8- cineole and camphor. All lavender oil is used in aromatherapy [8].

Lavender oil also can use in oral administration also can use in inhalation [9] also it can be used in massage [10].

Sebai [11] reported that lavender oil can protect against diabetes and oxidative stress. Lavender oil can use in thyroid health.

Not only is oxidative stress associated with thyroid dysfunction, but diabetes and other metabolic disorders have a complex relationship with butterfly – shaped gland too.

Korean scientists found that the use of lavender oil alleviates insomnia, improves self-satisfaction with sleep and it successfully addresses depression [12]: Lavender has a calming effect and it can prevent consequences associated with unmanaged stress.

Beside antioxidant property and antidiabetic effects of the lavender oil also it has anti-inflammatory properties [13]. It also can treat thyroid gland and promotes hair growth [14].

Coronary heart diseases can be measured by the lipid panel [15]. In all the four stages of breast cancer lipid profile significantly increased, while the values of VLDL and HDL-C were not significantly changed [16].

Cancer and cardiovascular diseases in developed countries are the leading causes of death [17]. The common risk factors of the cancer are lifestyle, obesity and high-fat diets, while cardiovascular diseases are affected by lipid profile as results of unhealthy diet as well as physical inactivity [18].

Cellular structure and function are affected by cholesterol which considers as a precursor to biochemical pathways, especially the synthesis of steroid hormones, which plays an important role in breast [19,20].

There are many explanations for the inverse relationship between dyslipidemia and breast cancer. HDL-C has beneficial effect supposed to be related to anti-inflammatory and anti-oxidative properties. It was reported that HDL-C can prevent lipid peroxidation through inhibiting low-density lipoprotein cholesterol oxidative damage [21,22]. Moreover, increasing of HDL-C in serum resulted in a great production of anti-inflammatory cytokines as interleukin 10 which plays a protective role against breast cancer [23].

2. MATERIALS AND METHODS

2.1 Chemicals

Doxorubicin hydrochloride (Adriadox 50 mg in 25 ml sterile water production of Royal Medical PVT. LTD Khandelwal laboratories PVT. LTD. Calculations of Doxorubicin (DOXO) dose for rats was performed according to Hidalgo et al. [24]: briefly, to convert a dose from mg/m^2 to mg/kg in human = 75 mg/m^2 (DOXO) in human =75÷37=2.02 mg/kg in human. To convert this dose from human to rats: 2.02 mg/kg in human=2.02×6.2=12.56 mg/kg in rats. Lavender oil, *Eruca sativa* oil and *Aloe vera* oil were obtained from Everline Natural oils and cosmetics Co., 6th October City. Cairo- Egypt saved in dark bottles and used fresh.

2.2 Induction of Mammary Tumours in Rats

All treated groups (four groups) and positive control are induced with breast cancer cell line MCF7 through injection of 1 ml of the cell line intraperitoneally (i.p.) and left for one month for the development of breast cancer.

Thirty female albino rats (Sprague Dawley) weighing about 160 gm ± 10 gm (purchased from the National Research Center, Dokki, Cairo-Egypt, are divided equally into six groups: group one served as non-treated negative control; group two was a cancer positive control which was induced with breast cancer MCF7 cell line (each rat was injected with 1 ml of this cell line 6* 10^6cell [25]; group three, was administered with 1 ml of sodium carbonate solution 1.2% solution (the dose in human used by some scientists was 12 g/L); rats of group four are administered with 1 ml of *Eruca sativa* oil; group five are administered with 1 ml lavender oil. Group six was administered with 1 ml *Aloe vera* oil notice that all used oils were water extract.

After that, rats of groups three, four, five and six were injected intraperitoneally with the chemotherapy doxorubicin hydrochloride 1 ml (2 mg/ml) solution [25]. Then at the second day, the administration of different treatments was orally through a stomach tube for one month then all rats were sacrificed.

At sacrifice, blood was collected in EDTA tubes for complete blood count analysis with anticoagulant and the other part of the blood was collected and left to coagulate then blood was centrifuged at 3000 rpm [26] for 10 min to obtain serum which preserved at -4°C in Eppendorf for later biochemical analysis.

Breast cancer cell line MCF7 was obtained from tissue culture VACSERA. Every rat was injected with 6X10^6 cells according to preliminary studies.

2.3 Biochemical Analysis

Determination of lipid profile:

Cholesterol

Cholesterol was assayed colourimetrically using Biodiagnostic kit and the method of Allain et al., [27].

Triglycerides

Triglycerides were measured colourimetrically using Biodiagnostic kit and method of Fossati and Prencipe [28].

HDL cholesterol

HDL cholesterol was assayed colorimetrically using Biodiagnostic Kit and the method of Lopes-Virella et al., [29].

LDL cholesterol

LDL cholesterol is assayed colorimetrically using Biodiagnostic Kit and the method of Wleland and Seldel [30].

VLDL

VLDL was calculated from the equation
VLDL=Triglycerides/5

LDH

LDH activity was measured using Abcam colorimetric kit (ab102526) according to the method of Zou et al., [31].

Creatin kinase MB

Creatin kinase MB (MB) was achieved according to the method of Tietz [32] using spectrum kit and measured colorimetrically.

Creatin kinase activity

It was determined colorimetrically using abcam kit (ab155901) according to the method of Luptak et al., [33].

Alfa-fetoprotein

Alfa-fetoprotein was achieved according to the method of Smith and Kelleher [34] using Invitrogen Alpha fetoprotein ELISA kit (EHAFP) for human.

Ca15–3

CA15-3 was achieved according to the method of Luftner et al., [35], using Invitrogen CA15-3 ELISA kit (99-0069) for human.

2.4 Statistical Analysis

Data statistically analyzed using ANOVA one way Followed by L.S.D. Using Graph pad Prism Program Version 7.

3. RESULTS

As in Table 1, using ANOVA data show high significant difference in total cholesterol between different treatments where using LSD as post hoc test data show significant decrease in total cholesterol in *Eruca sativa* oil, lavender oil and *Aloe vera* oil groups comparing to positive control. Where mean ± SD were, (76.52 ± 4.50) for positive control, (65.22 ± 7.00) for sodium carbonate, (59.20 ± 6.92) for *Eruca sativa* oil, (56.60 ± 4.58) for Lavender oil and (61.96 ± 10.58) for *Aloe vera* oil group.

As in Table 1, using ANOVA data show high significant difference in serum Triglycerides between different treatments were using LSD as post hoc test data show a significant decrease in serum triglycerides in *Eruca sativa* oil group and *Aloe vera* oil group comparing to the positive control. Data show a decrease in triglycerides in *Eruca sativa* oil, lavender oil and *Aloe vera* oil comparing to sodium carbonate group. Where mean ± SD was, (66.60 ± 14.50) for positive control, (69.60 ± 17.21) for sodium carbonate, (33.00 ± 1.00) for *Eruca sativa* oil, (52.00 ± 18.68) for Lavender oil and (45.3 ± 7.63) for *Aloe vera* oil.

As in Table 1, using ANOVA data show a high significant difference in serum HDL level between different treatments. Where data show a significant increase in HDL cholesterol in *Eruca sativa* oil group comparing to positive control. Where *Eruca sativa* oil, Lavender oil and *Aloe vera* oil groups increase HDL more than sodium carbonate. Where mean ± SD were, (20.60 ± 2.08) for positive control, (17.00 ± 0.10) for sodium carbonate, (25.30 ± 2.50) for *Eruca sativa* oil, (23.60 ± 3.50) for Lavender oil and (23.30 ± 5.02) for *Aloe vera* oil.

As in Table 1, using ANOVA Data show a very high significant difference between different treatments where, *Eruca sativa* oil, Lavender oil and *Aloe vera* oil show a significant decrease in LDL cholesterol comparing to the positive control. Where mean ± SD was, (42.60 ± 4.15) for positive control, (34.30 ± 11.01) for sodium carbonate, (27.30 ± 6.10) for *Eruca sativa* oil, (22.60 ± 6.02) for Lavender oil and (29.60 ± 3.50) for *Aloe vera* oil.

As in Table 1, using ANOVA data show a significant difference between different treatments were using LSD data show a significant decrease in s.VLDL-cholesterol in *Eruca sativa* oil group compared to positive control and comparing to sodium carbonate and Lavender oil groups. Where mean ± SD was, (13.32 ± 4.03) for positive control, (13.92 ± 3.04) for, sodium carbonate, (6.60 ± 0.54) for *Eruca sativa* oil, (10.40 ± 2.00) for Lavender oil and (9.06 ± 0.54) for *Aloe vera* oil.

As in Table 1, using ANOVA data show very high significant difference between different treatments where using LSD, LDH shows a significant increase in *Aloe vera* oil group comparing to positive control and comparing to other groups. Where mean ± SD was, (2395.30 ± 40.00) for positive control, (2425.30 ± 321.00) for sodium carbonate, (2359.30 ± 290.00) for *Eruca sativa* oil, (2361.30 ± 59.00) for Lavender oil, and (3602.30 ± 336.00) for *Aloe vera* oil.

As in Table 1, using ANOVA data did not show any significant difference in CK-MB.

As in Table 1, using ANOVA data show a significant difference between different treatments but LSD show the difference is between negative control and different groups in Creatin phosphokinase. Where mean ± SD was, (4596 ± 3089.00) for positive control, (5055.30 ± 1248.00) for sodium carbonate, (3249 ± 86.00) for *Eruca sativa* oil, (3227.3 ± 55.00) for Lavender oil, and (4926 ± 1629.00) for *Aloe vera* oil.

As in Table 2, using ANOVA data show a high significant difference between different groups were using LSD sodium carbonate show a significant decrease in serum alpha fetoprotein comparing to positive control also lavender oil group and *Eruca sativa* decreases serum alpha feto protein comparing to *Aloe vera*. Where mean ± SD were, (0.5 ± 0.00) for positive control, (0.3 ± 1.00) for sodium carbonate, (0.36 ± 0.05) for *Eruca sativa* oil, (0.4 ± 0.10) for Lavender oil, and (0.43 ± 0.05) for *Aloe vera* oil.

As in Table 2,using ANOVA data show very high significant difference between different groups where using LSD sodium carbonate, *Eruca sativa* oil and lavender oil groups show significant decrease in S. CA15-3 where sodium carbonate show significant decrease comparing to *Eruca sativa* and *Aloe vera* oil groups. Where mean ± SD were, (0.86 ± 0.05) for positive control, (0.56 ± 0.05) for sodium carbonate, (0.70 ± 0.10) for *Eruca sativa* oil, (0.65 ± 0.70) for Lavender oil, and (0.75 ± 0.21) for *Aloe vera* oil.

4. DISCUSSION

Eruca sativa (jarjeer) is an annual herb (family Brassicaceae), which contains a wide range of chemicals and minerals with nutraceutical and organoleptic characteristics. Jarjeer was generally used as a food and traditionally mainly consumed due to its aphrodisiac properties. This crop is known to contain various phytochemicals such as flavonoids, phenolic acids, terpens, carotenoids, tannins, glycosides, saponins, sterols, alkaloids, and other secondary metabolites. In leaves, kaempferol and its derivatives, glucosativin, are the main flavonoids and glucosinolate, respectively, while erucic acid and glucoerucin are the main fatty acid and glucosinolate, respectively. Medicinally, the plant has antibacterial, antidiabetic, antihypertensive, antiplatelet, and antioxidant activity and stimulates hair growth and other effects [36]. *Eruca sativa* extracts may appear their protective and treatment effect against oxidative damage result by rising/preserve the grade of antioxidant enzymes and antioxidant molecules [37].

Cancer changes lipid level [38] also, low-density lipoprotein and high cholesterol level are affected in cardio-vascular disease and consider the risk factor in different types of cancer [39].

Lipoproteins and cholesterol high levels are relating to breast cancer while the lowest levels are present in gastric cancer [40]. Low HDL is associated with breast cancer risk [41]. The increase of serum triglycerides is associated with colon cancer [42]. Cancer is a common disease and causes death [43]. Cardiovascular disease is the second disease cause death after cancer [44].

Doxorubicin is a cardiotoxic anthracycline because it has the ability to invoke reactive oxygen species production and lipid peroxidation and because of an excessive release of cytochrome C, which induces apoptosis [45].

Cardiotoxicity occurs by anthracycline; doxorubicin plays an important role in an increased risk of cardiovascular disease in breast cancer patients by alterations in the function of the heart [46]. Also, chemotherapy agents may alter other significant cardiovascular disease risk factors, in addition, its effect on plasma levels of lipids where there is an increase in total cholesterol and LDL in chronic myeloid leukemia [47].

In cardiovascular disease, there is a reduced HDL-C [48]. Doxorubicin is anthracycline to inhibit DNA and RNA synthesis. Some inflammatory genes are increased due to doxorubicin treatment. Also it used in treat of several cancers like breast, lung, gastric, thyroid, ovarian and others [49].

4.1 Mechanism of Anticancer Pharmacodynamics

The mechanisms by which doxorubicin is acting are 1- intercalation into DNA and disruption of topoisomerase II mediated DNA repair 2- generation of free radicals and their damage to cellular membranes, DNA and proteins [50].

Semi quinone which is an unstable metabolite, produced from doxorubicin oxidation it is converted back to doxorubicin in a process that release reactive oxygen species this reactive oxygen species can cause lipid peroxidation and membrane damage, DNA damage and cause apoptosis [51].

Table 1. Effect of sodium carbonate, *Eruca sativa* oil, lavender oil and *Aloe vera* oil on lipid profile and some heart function tests in breast cancer induced doxorubicin treated female albino rats

Groups / Parameters		Negative control (a)	Positive control (b)	Sodium carbonate (c)	*Eruca sativa* (d)	*Lavender* (e)	*Aloe vera* (f)	probability	ANOVA
S. Total cholesterol	Mean	79.76	76.52	65.22	59.2[ab]	56.60[ab]	61.96[ab]	0.01	**
	±SD	10.44	4.50	7.00	6.92	4.58	10.58		
S. Triglycerides	Mean	74.30	66.60	69.60	33.00[abc]	52.00[ac]	45.30[abc]	0.01	**
	±SD	9.01	14.50	17.21	1.00	18.68	7.63		
S.HDL-cholesterol	Mean	18.60[def]	20.60[d]	17.00[def]	25.30	23.6	23.3	0.01	**
	±SD	1.14	2.08	1.00	2.50	3.5	5.02		
S.LDL-cholesterol	Mean	46.3	42.6	34.3[a]	27.30[ab]	22.60[abc]	29.60[ab]	0.001	***
	±SD	7.09	4.15	11.01	6.10	6.02	3.50		
S.VLDL - cholesterol	Mean	14.86	13.32	13.92	6.60[abce]	10.40	9.06[a]	0.05	*
	±SD	2.00	4.03	3.04	0.54	2.00	0.54		
S. LDH	Mean	3018.00[f]	2395.30[af]	2425.30[af]	2359.30[af]	2361.30[af]	3602.30	0.001	***
	±SD	338.00	40.00	321.00	290.00	59.00	336.00		
S.CK-MB	Mean	1546.30	1591.30	1528.00	1656.00	1591.50	1581.00	0.05	N.S
	±SD	91.63	43.93	66.30	9.00	70.00	56.56		
S. Creatin phosphokinase	Mean	7386.6	4596.00[a]	5055.30[a]	3249.00[a]	3227.30[a]	4926.00[a]	0.05	*
	±SD	64.00	3089.00	1248.00	86.00	55.00	1629.00		

The small letters when be present in a group means that group has significant difference comparing to the groups taking the same letters in the head of the table

Table 2. Effect of sodium carbonate, *Eruca sativa* oil, lavender oil and *Aloe vera* oil on some tumor markers in breast cancer-induced doxorubicin treated female albino rats

Groups / Parameters		Negative control (a)	Positive control (b)	Sodium carbonate (c)	*Eruca sativa* (d)	Lavender (e)	*Aloe vera* (f)	probability	ANOVA
S. Alfa-Feto protein	Mean	0.23bdef	0.50	0.30bef	0.36f	0.40f	0.43	0.001	***
	±SD	0.05	0.00	0.10	0.05	0.10	0.05		
S. CA 15-3	Mean	0.43bcdef	0.86	0.56bdf	0.70b	0.65b	0.75	0.001	***
	±SD	0.05	0.05	0.05	0.10	0.70	0.21		

The small letters when be present in a group means that group has significant difference comparing to the groups taking the same letters in the head of the table

4.2 Mechanism of Cardiotoxicity

The mechanism of cardiotoxicity of doxorubicin is through iron related free radicals and formation of doxorubicinol as a metabolite [52].

This study shows the following results: *Eruca sativa* oil, Lavender oil and *Aloe vera* oil decreases total cholesterol compared to positive control. *Eruca sativa* oil and *Aloe vera* oil decreases triglycerides comparing to positive control. *Eruca sativa* oil increases HDL-C comparing to positive control. *Eruca sativa* oil, Lavender oil, *Aloe vera* oil decreases S.LDL-C comparing to the positive control. *Eruca sativa* oil decreases VLDL-C comparing to control. *Aloe vera* oil decreases S.LDH comparing to positive control. Sodium carbonate decreases S-Alpha fetoprotein comparing to positive control in addition, Sodium carbonate, *Eruca sativa* oil and Lavender oil decreases Ca15-3.

Administration of *Eruca sativa* extracts resulted in a decrease in serum triglycerides, LDL, VLDL and increase of HDL-C in a contrary manner. The oncofetal antigen found in most types of cancer is the alpha-fetoprotein [53].

The major fetal serum protein is alpha-fetoprotein [54,55] which synthesized mainly by the liver and yolk sac. Alpha-fetoprotein level drops sharply and disappearing from the blood of normal adults [56]. When tissue and embryonic cells reach a high degree of differentiation, the alfa-fetoprotein uptake ceases, even if the concentration of alpha-fetoprotein in blood still high or increasing [57].

The malignant cells still able to regain take up alpha-fetoprotein via a receptor that would be present in undifferentiated cells of embryonic and tumour origin [58]. Alpha-fetoprotein can use to diagnose cancer.

Anthracyclines have side effects like alopecia, emesis, and mucositis in addition to cardiotoxicity and secondary leukemias and necrosis [59].

Anthracyclines cause loss of muscle fibres from myocytes by action of dilated sarcoplasmic reticulum and cytoplasmic vacuolization [60].

Adriamycin used in metastatic and early breast cancer but it has cardiovascular toxicity [61].

Cruciferous vegetables reduce risk of development of cancer this is attributed to isothiocyanates. Erucin is a material present in rocket salad which is related to sulforaphane it acts through induction of apoptosis and ROS-mechanisms [62]. Diet rich in cruciferous vegetables have a beneficial effect on cancer [63].

Most cancers like lung, prostate, breast and colon cancer can be treated with cruciferous vegetables which include glucosinolates and isothiocyanates [64].

Rocket salad is one of the cruciferous vegetables it includes phytochemicals and used in the Mediterranean diet [65]. Rocket salad includes many antioxidants like polyphenols, vitamin and carotenoids, in addition, it characterized by high glucosinolate content and isothiocyanates which effect on cancer cell growth [66,67].

Rocket species is used as diuretic, digestive emollient tonic, stimulant, depurative, laxative and rubefacient [68] in addition seeds have antidiabetic effect and reduces oxidative stress [69]. *Eruca sativa* extract reduces nephrotoxicity [69] and have antigenotoxic effect and antiulcer properties [70,71].

Erucin has anticancer effect through induction of detoxification enzymes in mouse tissues [72]. These findings are confirmed in human and rat tissues [73], also Erucin has effect on cell cycle, growth inhibition, regulation and apoptosis induction in most cancers [74].

Erucin induces a strong ant proliferative effect on human leukemia cells [75]. It also has the same biological activities of sulforaphane [76].

Oxidative stress responsible for production of free radicals, which involved in the chronic disease. These diseases can improve by dietary antioxidants. Rocket salad considers good dietary antioxidants [77].

Erucin has direct antioxidant capacity and also indirect antioxidant capacity through the an indication of cellular antioxidant systems like the thioredoxin reductase 1 as in human breast cancer MCF-7 cells [78]. Phenyl ethyl isothiocyanate killed transformed cells by increasing ROS production which leads to cell cycle arrest and apoptosis thereby prevents cancer cell proliferation [79].

Eruca sativa green leaves include range of phytochemicals, flavonoids and glucosinolates which reduce risk of cardiovascular diseases and many types of cancers [80].

Doxorubicin used to treat metastatic breast cancer, the median time for survival is approximately 2 years [81].

The most common cancer among women is the breast cancer which is the cause of mortality and morbidity for women worldwide [82]. The extra cellular microenvironment of most solid tumors is acidic [83].

Martinez-Zaguilan et al., [84] reported that acidity of tumor may derive malignancy because it direct enzymes as metalloproteases MMP1, MMP2 and MM-9 and lysosomal proteases as Ca the spin B, D or L [85].

PH of tumors can rise by administration of alkaline agent [86]. This findings are agree at least in some tumor types, which where systemic alkalinization reduces metastasis spread and improves survival [87]. *Eruca sativa* used as antioxidant and antimicrobial agent [85].

The mechanism of anti-carcinogenic activity of isothiocyanates has not yet been fully elucidated. Isothiocyanates reduce activation of carcinogens and increase their detoxification finally exhibiting anti-carcinogenic activity [84].

Essential oil includes many compounds like monoterpenes, aldehydes, esters, ketones, phenols, alcohols and oxides which are volatile and may produce characteristic odors [88].

Doxorubicin used in cancer therapy since long. Despite it has broad –spectrum antineoplastic activity, adverse action especially cardio toxicity has limited its usage [89].

The cardio toxicity associated with conventional doxorubicin is broadly classified as either acute or chronic [90].

The Cardiovascular toxicity is a dose limiting. Risk factors that may increase the occurrence of cardio toxicity include previous or current heart disease, extremes in age, race exposure to irradiation in the mediastinal region and the cumulative dose of doxorubicin received. Patients with acute doxorubicin-induced cardio toxicity present with rhythm disturbance [91].

Theoretically a pro-atherosclerosis happens when metabolic acidosis occurs which promote LDL oxidation by shortening the lag phase of oxidation [92].

It is fairly established that a reduction of lipolysis is associated with a reduction in pH (increasing acidity) [93] and some evidence to suggest that with lipolysis there is inverse effect a mild alkalosis (increase in pH) [94] this is observed at the rest, but bicarbonate administration during exercise does not alter rates of lipolysis.

Lactic acid and lactate responsible for a balance within the body. Lactate can dissociate into lactic acid plus a free hydrogen ion to decrease PH in tissues [95].

When sodium bicarbonate (200-500 mg/kg) is ingested prior to short power exercises lactate is increased relative to control [96].

Bicarbonate administration decrease cellular acidity that results from metabolic processes [97].

The slow phase of pulmonary Vo_2 (Pvo_2) kinetics can altered by sodium bicarbonate ingestion (for an aerobic exercise, highly associated with muscle energy turnover [98], without affecting the fast phase [99].

4.3 Cytochemical Constituents of *Aloe vera*

Nearly all parts of the plant have some pharmacological properties. The leaves are diuretic, anti-scorbutic, stimulant and stomachic. The seed is stimulant and rubefacient. The rocket oil also has methylsulphonylbutyl isothiocyanate and glucosinolate which induces enzymes activity. All phytochemicals found in seeds are responsible for antimicrobial action against various microorganisms. Phenolic compounds present in the seeds have antimicrobial properties against bacteria [100]. Tannins have antiviral, antibacterial and anti-tumor action also used as diuretic in addition saponin precipitate and coagulates red blood cells.

Rocket contains, Lutein, B-carotene and z exanthema, fat-soluble carbonoid pigments that act as antioxidants and prevent cancer and macular degeneration. Rocket includes natural antioxidants like vit.C, K and A and fight free radical activity, these vitamins support the immune system. Vitamin A and flavonoid protect the body from skin , lung and oral cancer [101].

Eruca sativa extract have flavonoids glucoerucin which playing role in scavenging oxygen species (ROS) and reactive nitrogen species (RNS) [102].

The genus *Lavandula* agriculated in Mediterranean Sea area. It includes more than 30, Lavender oil includes many antioxidant molecules and it has strong antioxidant action against lipid peroxidation and antibacterial activity. The essential oil is camphor, Eucalyptol, 1, 5-Dimethyl-1 vinyl 4- hexenyl butyrate, 1, 3, 7-Octatriene, 3, 7- dimethyl [103].

Lavender oil includes Linalol and Linalyl acetate it has antimutagenic activity in addition to antioxidant properties [104]. Phytochemical studies revealed that Linalool, Linalyl acetate and some other monoterpene and sesquiterpenes, Flavonoids like Luteolin, Triterpenoids like Ursolic acid and coumarins like Umbelliferone and coumarine were main components of the aerial parts and flowers of *Lavandula* which might be effective on serum lipids levels [105]. This plant possesses high levels of polyphenol compounds having antioxidant properties. Antioxidants are effective in prevention and treatment of cardiovascular diseases, particularly atherosclerosis [106].

5. CONCLUSION AND RECOMMENDATION

1- Lavender oil, *Eruca sativa* oil and *Aloe vera* oil decreases total cholesterol.
2- *Eruca sativa* oil and *Aloe vera* oil decreases triglycerides
3- Lavender oil, *Eruca sativa* oil and *Aloe vera* oil decreases triglycerides comparing to sodium carbonate
4- Lavender oil, *Eruca sativa* oil and *Aloe vera* oil increases LDL more than sodium carbonate
5- Lavender oil, *Eruca sativa* oil and *Aloe vera* oil decreases LDL
6- *Eruca sativa* oil decreases VLDL
7- *Aloe vera* increases LDH
8- Sodium carbonate decreases alpha fetoprotein. Where, *Eruca sativa* oil and Lavender oil have extra effect than *Aloe vera*
9- *Eruca sativa* oil Lavender oil and sodium carbonate decreases Ca15-3 and sodium carbonate have extra effect than *Eruca sativa* oil and *Aloe vera* oil.

5.1 Recommendation

We recommend with using lavender oil, *Eruca sativa* oil, *Aloe vera* oil and sodium carbonate with low doses as helper cure with chemotherapy in treatment of breast cancer because it has useful effect in decreasing tumor markers and lipids and improve heart properties.

ETHICAL APPROVAL

All animals received human care in compliance with the standard institution's criteria for the care and use of experimental animals according to ethical committee of faculty of science, Al Azhar University.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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