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BIOLOGICAL AND HISTOPATHOLOGICAL STUDIES ON SOME HERBS MIXTURE IN OBESE RATS

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ABSTRACT: *The effects of herbs mixture at different levels of mixture components (Thymus, Fennel and Phyllanthus on some biological and histological factors of hyperlipidemic obese rats were studied. Thirty adult female rats were distributed into five groups, the first one was kept as negative control, while the other four groups were fed on high fat diet for induction of obesity. One of these groups was kept as positive control while the left 4 groups were given daily by 20% mixture of Thymus, Fennel and Phyllanthus at 10,5, 5% mixture, 5,10,5% mixture and 5,5,10% mixture for 4 weeks. Results showed that body weight gain was markedly lower especially in the mixture of Thymus, Fennel and Phyllanthus (5,5 and 10%) compared to high fat diet control group. Also, their mixture at 5,5 and 10% lowered concentrations of total cholesterol, triglycerides, LDL-c, VLDL-c and decreased activity of AST and ALT enzymes. Furthermore, all mixture caused significant increase in HDL-c and T3 hormone concentrations except mixture (1) Thymus, Fennel and Phyllanthus at 10,5 and 5% .*

Histopathological examination showed amelioration of histopathological lesions seen in liver of obese rats received the mixture of herbs at different levels. This study recommends that intake of the mixture of Thymus, Fennel and Phyllanthus especially at 5,5 and10% respectivelly because it may be useful for treating obesity.

Key words: *Obese rats, Thymus, Fennel and Phyllanthus, serum lipids, histopathology.*

INTRODUCTION

Obesity is a complex problem resulting from an imbalance between energy intake and energy expenditure with genetic, metabolic and behavioral components. Obesity is defined as an excessive fat accumulation in the body that presents a risk to health.Despite a major contribution of genetic susceptibility, the rapid development of the obesity must reflect substantial changes in other factors such as diet (Archer *et al*., 2007). In particular, increases in the amount of fat in the diet have been shown to be associated with the risk of obesity and hyperlipidemia in human and rodents by altering cholesterol and triglyceride levels in plasma and tissues. Hyperlipidemia is known to enhance the risk of coronary heart disease, fatty liver disease and carcinogenesis, which is associated with reactive oxygen species formation (Roberts *et al*., 2006). In recent years, many studies have focused on the bioavailability of phenolic compounds in the prevention and treatment of obesity. Phenolic compounds and flavonoids have pharmacological properties such as antioxidant, antimutagenic, antithrombotic, antiinflammatory, anticancer and antihyperlipidemic. They are widely distributed in plants and form part of the human diet (Son and Lewis, 2002).

Thyme is an herb. The flowers, leaves, and oil are used as medicine. Thyme is sometimes used in combination with other herbs. Thyme is taken by mouth for bronchitis, whooping cough, sore throat, colic, arthritis, pset stomach, stomach pain (gastritis), diarrhea, bedwetting, a movement disorder in children (dyspraxia), intestinal gas (flatulence), parasitic worm infections, and skindisorders. It is also used to increase urine flow (as a diuretic), to disinfect the urine, and as an appetite stimulant. Some people apply thyme directly to the skin for hoarseness (laryngitis), swollentonsils (tonsillitis), sore mouth, and bad breath.Thyme oil is used as a

germ-killer in mouthwashes and liniments. It is also applied to the scalp to treat baldness and to the ears to fight bacterial and fungal infections.Thymol, one of the chemicals in thyme, is used with another chemical, chlorhexidine, as a dental varnish to prevent tooth decay.In foods, thyme is used as a flavoring agent. In manufacturing, red thyme oil is used in perfumes. It is also used in soaps, cosmetics, and toothpastes. Thyme contains chemicals that might help bacterial and fungal infections, and minor irritations. It also might relieve smooth muscle spasms, such as coughing. Thyme contains many active principles that are found to have disease preventing and health promoting properties. thymol, one of the important essential oils, which scientifically has been found to have antiseptic, anti-fungal characteristics. The other volatile oils in thymeinclude carvacolo, borneoland geraniol. flavonoid phenolic antioxidants like *zea*-xanthin, lutein, pigenin, naringenin, luteolin, and thymonin. Fresh thyme herb has one of the highest antioxidant levels among herbs, a total ORAC (Oxygen Radical Absorbance Capacity) value of 27426-µmol TE/100 g.Thyme is packed with minerals and vitamins that are essential for optimum health. Its leaves are one of the richest sources of potassium, iron, calcium, manganese, magnesium, and selenium. Potassium is an important component of cell and body fluids that helps controlling heart rate and blood pressure. Manganese is used by the body as a co-factor for the antioxidant enzyme, superoxide dismutase. Iron is required for red blood cell formation. The herb is also a rich source of many important vitamins such as B-complex vitamins, beta carotene, vitamin A, vitamin K, vitamin E, vitamin C and folic acid. Thyme provides 0.35 mg of vitamin B-6 or pyridoxine; furnishing about 27% of daily recommended intake. Pyridoxine keeps up GABA (beneficial neurotransmitter in the brain) levels in the brain, which has stress buster function. Vitamin C helps the human body develop resistance against infectious agents and scavenge harmful, pro-inflammatory free radicals.Vitamin A is a fat-soluble vitamin and antioxidant that is required maintaining healthy mucus membranes and skin and is also essential for vision. Consumption of natural foods rich in flavonoids like vitamin A and beta-carotene helps protect from lung and oral cavity cancers Vági *et al*., (2005); Yassin *et al*., (2007) and Amarowicz *et al.,* (2008).

Fennel is an herb native to southern Europe and Asia Minor. Fennel contains anethole, which can explain some of its medical effects: It, or its polymers, act as phytoestrogens. The essence of fennel can be used as a safe and effective herbal drug for primary dysmenorrhea, but could have lower potency thanmefenamic acid Fennel is widely employed as a carminative, both in humans and in veterinary medicine (e.g., dogs), to treat flatulence by encouraging the expulsion of intestinal gas. Anethole is responsible for the carminative action. It also serves as a mild laxative. On account of its aromatic and carminative properties, fennel fruit is chiefly used medicinally with purgatives to allay their tendency to griping and for this purpose forms one of the ingredients of the well-known compound Liquorice Powder. Fennel water has properties similar to those of anise and dill water: mixed with sodium bicarbonate and syrup, these waters constitute the domestic 'gripe water', used to correct the flatulence of infants. Volatile oil of Fennel has these properties in concentration. Fennel tea, formerly also employed as a carminative, is made by pouring half a pint of boiling water on a teaspoonful of bruised fennel seeds. Fennel can be made into a syrup to treat babies with colic (formerly thought to be due to digestive upset), but long-term ingestion of fennel preparations by babies is a known cause of thelarche (Cani *et al*., (2005) and Urias-Silvas *et al*., (2007).

The herb *Phyllanthus emblica* has gained interest as a potential treatment for human bone disorders] as well as diabetes patients. Gaining attention for its potential effects against hepatitis B, research on Phyllanthus niruri has revealed possible antiviral activity also against human immunodeficiency virus (HIV). Phyllanthus plants have been used

in folk medicine used to treat a wide number of diseases. In Indian Ayurvedic medicine, various herbaceous Phyllanthus species are known as*bhuiamla*, a name previously assigned to *P. niruri* only. Bhuiamla is prescribed for jaundice, gonorrhea and diabetes (internaluse) as well as poultices, skin ulcer and other skinproblems (external use). Infusions are made from young shoots as a treatment of chronic dysentery. Not many of these supposed benefits, however, is established with modern scientific research (Gazzani *et al*., 2000).

The bark of *Phyllanthus muellerianus*, commonly called "mbolongo" in Cameroon, is used by pygmies as a remedy for tetanus and wound infections. *Phyllanthus muellerianus* extracts are antimicrobial. *Phyllanthus niruri* may possibly help prevent stone formation/urolithiasis. *Phyllanthus amarus* root and leaf extract showed significant hepatitis C antiviral activity. *Phyllanthus* species for patients with chronic hepatitis B virus infection have been assessed in clinical trials, but no consensus regarding their usefulness exists. *Phyllanthus acidus* (leaf) showed antiplasmodial activity against *Plasmodium falciparum*. *Phyllanthus reticulatus* leaves showed potential RNase H inhibition and protection against the viral cytopathic effects of HIV-1. Leaves, roots, stem, bark and berries of this genus contain lignans (e.g. phyllanthin and hypophyllanthin) and a variety of other phytochemicals (Ahmed *et al*., 2003). It has also promising effects on the body weight and fat mass development. There are no scientific studies available on the effects of Both of *Thymus*, Fennel and Phyllanthus in obesity although these plants are widely used as a fork remedy for the treatment of obesity. Therefore the present work was designed to study the effects of the mixture of herbs at different levels on some biological, parameters and histopathological changes of obese rats.

MATERIALS AND METHODS

Thymus, Fennel and Phyllanthus were obtained from the local market of herbs and medicinal plants, Cairo, Egypt and scientifically identified at Horticultural Research Institute, Agriculture Research Center, Egypt. All chemicals and diagnostic kits were purchased from El-Gomhoria Co., Cairo, Egypt.

Experimental animals: This study was carried out on thirty adult female Sprague Dawley albino rats weighing 155-160 g body weight. The rats were obtained from Laboratory Animal Colony, Helwan, Egypt. Before their use in the experiment, the rats were kept for one week for acclimatization to the laboratory conditions. They were fed on basal diet and provided with water and food ad libitum.

Preparation of experimental diets and induction of obesity: Basal diet (AIN-93M) was prepared according to Reeves *et al*., (1993) which provide about 9.5% of its energy from fat (40 g corn oil/kg diet). In order to induce obesity, High Fat Diet (HFD) was used in which at least 45% of its energy comes from fat as reported by Bhatt *et al*., (2006). Basal diet was modified to contain 40 g corn oil + 200 g ghee/kg diet and the amount of add saturated fat was substituted from the amount of corn starch.

Experimental procedure: Rats were divided into five groups consisting of six rats each. The first group was fed on the high fat basal diet and kept as a control negative, while from the second to the fifths group, they were fed on HFD during the experimental period. After 6 weeks that was required to induce obesity as stated by Huang *et al*., (2004) and Bhatt *et al*., (2006) the second group was left as a control positive, while the rest were given mixture of herbs. During the experiment period, the food intake and body weight were weighed daily and twice a week, respectively. Body Weight Gain (BWG) and Food Efficiency Ratio (FER) were calculated at the end of the experimental period according to the following equations: BWG (g) = final weight (g) - initial weight (g) FER = weight gain (g)/food intake (g).

Collection of blood samples and organs: At the end of the experimental period, rats were sacrificed following a 12 h fast. The rats were lightly anaesthetized by ether and about 7 ml of blood was withdrawn from the

hepatic portal vein into dry centrifuge plastic tubes. Blood portal vein into dry centrifuge plastic tubes. Blood separate the serum samples which were kept in tubes at -20 C till biochemical analysis. Left and right inguinal adipose pads were removed and weighed. The sum of adipose pads to body weight, multiplied by 100, yielded adiposity index (Jeyakumar *et al*., 2006). In addition, livers of the sacrificed rats were removed for histopathological study.

Biochemical analysis: Serum total cholesterol was calorimetrically determined according to Allain *et al*., (1974) and triglyceride was determined calorimetrically according to Wahlefeld, (1974). High Density Lipoprotein cholesterol (HDL-c) was determined calorimetrically according to Richmond, (1973). Low Density Lipoprotein cholesterol (LDL-c) and Very Low Density Lipoprotein cholesterol (VLDL-c) were calculated mathematically according to Friedewald *et al*., (1972) LDL-c = TC-[HDL-c + (TG/5)] VLDL-c = Triglycerides/5.

The activity of Aspartate Aminotransferases (AST) and Alanine Aminotransferases (ALT) enzymes were assigned by the method of Bergmeyer *et al*. (1978). Thyroid hormones (free T4 and free T3) and thyrotrophin or Thyroid Stimulating Hormone (TSH) were estimated in serum using Radioimmunoassay (RIA) as described by Patrono and Peskar (1987).

Histopathological study: Livers of the scarified rats were dissected, removed, washed with normal saline and put in 10% formalin solution. The fixed specimens were then trimmed, washed and dehydrated in ascending grades of alcohol. The tissue specimens were cleared in xylene, embedded in paraffin, sectioned at 4-6 microns thickness, stained with Hematoxylen and Eosin (H and E) and then studied under an electronic microscope according to Carleton (1979).

Statistical analysis: Results are expressed as mean values with their standard deviation of the mean. Statistical differences between groups were evaluated using one-way ANOVA followed by Duncan post hoc test using SPSS version 11.0 for Windows (SPSS, Chicago, IL, USA). Differences were considered significant at ($p<0.05$) according to Snedecor and Cochran (1986).

RESULTS

Feed intake was lower in the HFD fed rats compared to normal diet fed rats and lower in the rats given the mixture of the herbs at 10,5,5% mixture(1), 5,10,5% mixture(2) and 5,5,10 % mixture(3) of *Thymus*, Fennel and Phyllanthus but the difference was not significant as shown in (Table 1). Body weight gain was markedly lower in the mixture herb group (5,5% and10% *Thymus*, Fennel and Phyllanthus) when compared to positive control group. At the end of the study, body weight gain of this group at mixture of *Thymus*, Phyllanthus and Fennel group (5,5% and 10%) was about 29%:35% lower compared to positive control group. Thus Food Efficiency Ratio (FER) was significantly lowered. FER of positive control group was higher than normal diet fed rats and lowered by giving the mixture of herbs to obese rats. Adiposity index of mixture of the herbs at different levels supplemented groups was significantly lower than that of positive control group.

Administration ofthe mixture of *Thymus*, Fennel and Phyllanthus at 5,5% and 10% caused significant decreases in serum levels of total cholesterol, triglycerides, LDL-c and VLDL-c compared to positive control group (Table 2). Serum HDL-c levels increased but not significantly by the administration of the mixture of *Thymus*, Fennel and Phyllanthus at 5,5% or 10%. Obese rats that were given mixture of *Thymus*, Phyllanthus and Fennel group (5,5% and 10%) showed significantly higher levels of HDL-c compared to positive control. These values resembled to that of negative control group.

The administration of mixture of *Thymus*, Fennel and Phyllanthus group (5,5% and 10%) significantly reduced AST level but it did not affect ALT level. On the other hand, administration of the other mixture of herbs at the levels 5,10,5 and 10,5,5 significantly reduced serum levels of AST and ALT enzymes in obese rats compared to positive control group (Table 3). More reduction in ALT enzyme was observed, that were not significant compared to negative control groups.

Table (1): Effect of mixture of *Thymus*, Fennel and Phyllanthus herbs on feed intake (FI),body weight gain (BWG), feed efficiency ratio (FER) and adiposity index in obese rats.

Groups FI	FI (g/day)	BWG (g/day)	FER	Adiposity index
Negative control	28.97±0.99c	2.42±0.49b	0.08±0.004a	0.46±0.031a
Positive control	21.75±1.87ab	2.77±.093c	0.13±0.014d	1.26±0.07e
Mixture (1)	20.95±1.57ab	2.30±0.13b	0.11±0.002c	1.10±0.10d
Mixture (2)	19.69±1.33a	1.79±0.11a	0.09±0.004ab	0.82±0.05b
Mixture (3)	19.59±1.05a	1.80±0.14a	0.09±0.006ab	0.78±0.03b

Values are mean±SD. Values in the same column sharing the same superscript letters are not statistically significantly different at ($p<0.05$)
Mixture 1: mixture of *Thymus*, Fennel and Phyllanthus group (10,5% and 5%)
Mixture 2: Mixture of *Thymus*, Fennel and Phyllanthus group (5,10% and 5%)
Mixture 3: Mixture of *Thymus*, Fennel and Phyllanthus group (5,5% and 10%)

Table (2): Effect of mixture of *Thymus*, Fennel and Phyllanthus herbs on serum lipids parameters (mg/dl) in obese rats.

Groups FI		TC	TG	HDL-c	LDL-c	VLDL-c
Negative control	Negative Control	100.67±2.08a	69.33±3.06a	50.27±6.81d	36.53±4.37a	13.86±0.61a
Positive control	Positive Control	160.20±9.23e	112.60±6.95d	28.36±5.57a	109.32±9.83e	22.52±1.39d
Mixture (1)	Phyllanthus at 5%	138.33±2.88d	91.67±4.51c	34.17±1.93ab	85.83±4.03d	18.33±0.90c
Mixture (2)	Mixture at 5%	110.33±5.03b	82.67±2.52b	40.67±5.51bc	53.13±5.76bc	16.53±0.50b
Mixture (3)	Mixture at 10%	111.00±5.48b	84.00±6.28bc	47.72±6.03cd	46.48±6.06ab	16.80±1.26bc

Values are mean±SD. Values in the same column sharing the same superscript letters are not statistically significantly different at ($p<0.05$)
Mixture 1: mixture of *Thymus*, Fennel and Phyllanthus group (10,5% and 5%)
Mixture 2: Mixture of *Thymus*, Fennel and Phyllanthus group (5,10% and 5%)
Mixture 3: Mixture of *Thymus*, Fennel and Phyllanthus group (5,5% and 10%)

Table (3): Effect of mixture of Thymus, Fennel and Phyllanthus herbs on serum levels of liver function enzymes in obese rats.

Groups FI	Groups	AST (U/L)	ALT (U/L)
Negative control	Negative Control	77.33±2.52a	23.67±4.81a
Positive control	Positive Control	128.2± 4.76f	33.80±4.43c
Mixture (1)	Phyllanthus at 5%	110.00±1.00e	32.67±2.51bc
Mixture (2)	Mixture at 5%	86.00±1.01b	26.01±1.01a
Mixture (3)	Mixture at 10%	88.20±2.39bc	23.80±1.64a

Values are mean±SD. Values in the same column sharing the same superscript letters are not statistically significantly different at ($p<0.05$)
Mixture 1: mixture of *Thymus*, Fennel and Phyllanthus group (10,5% and 5%)
Mixture 2: Mixture of *Thymus*, Fennel and Phyllanthus group (5,10% and 5%)
Mixture 3: Mixture of *Thymus*, Fennel and Phyllanthus group (5,5% and 10%)

From Table 4 it could be noticed that administration of the water extracts of phyllanthus at 5% and 10% did not affect free T4 activity. On the other hand, the mixture of herbs (5,5% and 10%) of *Thymus*, Fennel and Phyllanthus induced significant increases in serum levels of free T4 and T3 hormones compared to positive control group. All other tested mixture of herbs caused non significant changes in serum level of Thyroid Stimulating Hormone (TSH).

Histopathological examination of liver of the negative control rats fed on basal diet revealed normal histological picture of hepatic lobule which consists of central vein surrounded by normal hepatocytes as shown in (photo. 1. A). Examination of liver of positive control obese rats showed fatty degeneration of hepatocytes and infiltration of leucocytes in hepatic sinusoid (photo. 1. B). Liver of rats given the first mixture showed little vacuolar degeneration of hepatocytes and some improvement in fatty degeneration (photo. 1. C). In addition, portal edema and few leucocytes infiltration in hepatic lobule were observed the second mixture of herbs (photo. 1. D). Liver and the third mixture showed marked improvements with no observed pathological lesions (photo. 1. E).

DISCUSSION

Several studies have shown that each of thymus and phyllanthus extract contains considerable amounts of important compounds which may serve as antioxidants. For example, Yassin *et al.*, (2007) reported that thymus and fennel extract had high content of phenolics compounds (58.1mg/g), flavonoids (7.23 mg/g) and carotenoids (0.52 mg/g). Furthermore, Vági *et al.*, (2005) and Amarowicz *et al.*, (2008) found that phyllanthus ethanolic extract contain considerable amounts of total phenolics compounds and have antioxidant activity and free radical-scavenging capacity.

Table (4): Effect of mixture of Thymus, Fennel and Phyllanthus herbs on serum levels of thyroid hormones and Thyroid.

Groups FI	Free T3 (ng/dl)	Free T4 (ng/dl)	TSH (µg/L)
Negative control	75.73±5.96c	3.90±0.09c	0.005±0.002a
Positive control	65.75±5.55a	2.05±0.03a	0.004±0.002a
Mixture (1)	69.80±4.35b	2.15±0.03a	0.004±0.001a
Mixture (2)	72.76±4.35bc	3.12±0.03b	0.004±0.002a
Mixture (3)	71.80±3.63b	3.17±0.02b	0.005±0.001a

Values are mean±SD. Values in the same column sharing the same superscript letters are not statistically significantly different at ($p<0.05$)
Mixture 1: mixture of *Thymus*, Fennel and Phyllanthus group (10,5% and 5%)
Mixture 2: Mixture of *Thymus*, Fennel and Phyllanthus group (5,10% and 5%)
Mixture 3: Mixture of *Thymus*, Fennel and Phyllanthus group (5,5% and 10%)

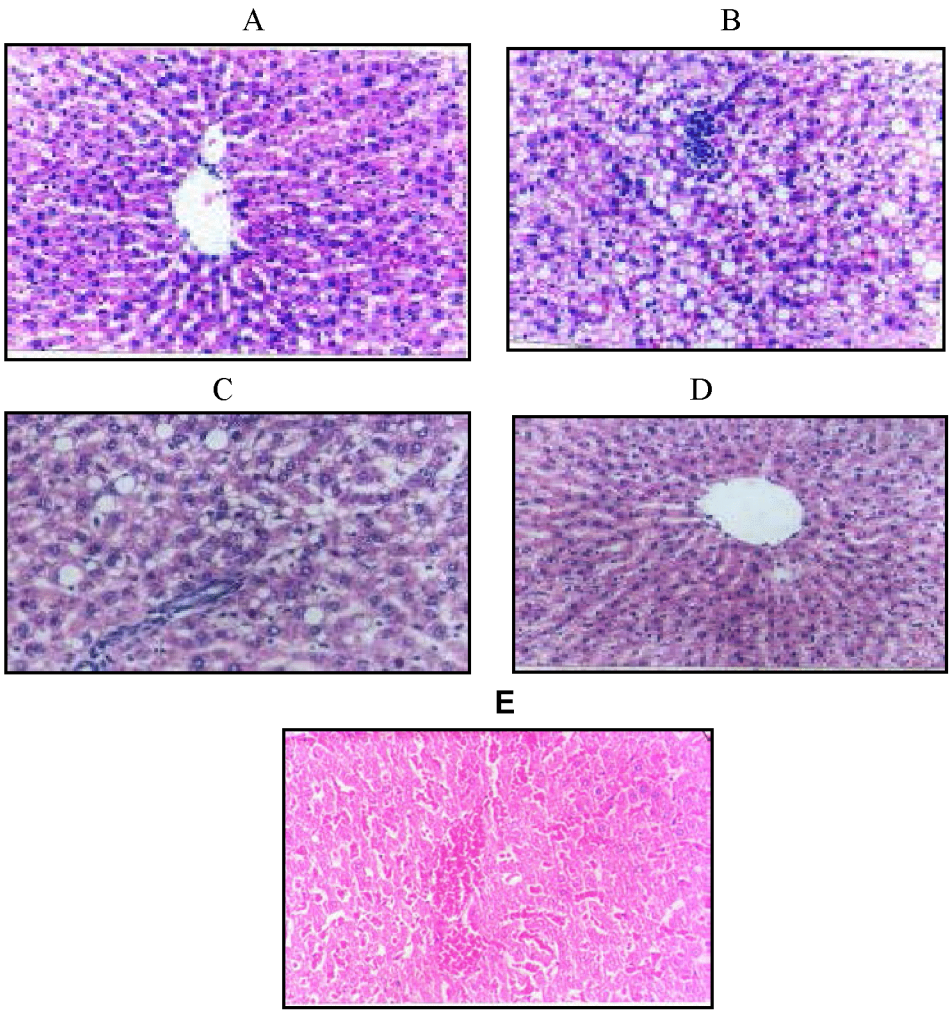

Photo. (1). Histopathological changes detected in the liver of (A) negative control, (B) positive control, (C) mixture 1 (D) mixture 2 and (E) mixture3

It is well-known from the literature that the main active compounds of thymus and fennel extract are inulin and fructooligosaccharides (Kocsis *et al*., 2003). Inulin is a polymer of fructose with ß-(2-1) glycosidic linkages (Wight and Niekerk, 1983). As it is water soluble and nothydrolysed by human digestive enzymes, it behaves like soluble fiber. It may increase the viscosity of the soluble fiber. It may increase the viscosity of the stomach content, which can slow down the rate of gastric emptying of water, nutrients and lipids, or it can cause alterations in hormone secretions, which affect lipid metabolism. The observed effect of thymus and fennel extract on food intake and body weight in this study was agreed with that reported by Cani *et al*., (2005) and Urias-Silvas *et al*., (2007) that the addition of oligofructose; a shortchain fructans obtained from thymus and fennel inulin; might enhance satiety, thereby resulting in greater reductions in energy intake and protects against the body weight gain, fat mass development in normal and obese rats.

The effect of herbal mixture of both phyllanthus, thymus and fennel on food intake and body weight could be attributed to the presence of inulin-type fructans of thymus and fennel herb in that mixture. In accordance with the present results, Yassin

et al., (2007) reported that thymus and fennel improve lipid profiles by lowering plasma total cholesterol and triglyceride concentrations while Ninfali *et al.*, (2005) reported similar results for phyllanthus. The hypocholesterolemic effect of phyllanthus ,thymus and fennel herbs could be attributed to presence of isoflavones in both herbs which prevent intestinal absorption of cholesterol by competition for its absorption sites as mentioned by Rang and Dale (1991).

The potent hypercholesterolemic and hypotriglyceridemic effects of thymus and fennel extract could be due to the presence of inulin which behaves like a soluble fiber and possesses hypolipidemic effect (Lairon, 1996). On the other hand, in Kim and Shin (1998) study, serum total cholesterol and triglyceride concentrations were not significantly affected by thymus and fennel or inulin feeding. The difference in the cholesterolemic effect of similar dietary fibers among different studies may be due to the percentage of added dietary cholesterol, the presence or absence of cholic acid, the level of dietary fiber and species.

The results of serum lipoproteins were coincide with that of Kim and Shin (1998) who reported that feeding rats on diets containing 5% thymus and fennel or 5% inulin for 4 weeks resulted in higher serum concentration of HDLc and lower serum concentration of LDL-c. In addition, Yassin *et al.*, (2007) stated that HDL-c concentration was significantly elevated in thymus , fennel and phyllanthus at 5,5 and 10% group than in normal control or high fat group.

The observed elevation of Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST) in high fat fed groups (obese groups) may be attributed to the incidence of fatty liver which is a metabolic consequence of obesity (Angulo, 2002; Angelico *et al.*, 2003). Moreover, Clark *et al.*, (2003) and Clark and Diehl (2003) reported that fatty liver is commonly associated with long term elevations in liver enzymes. The reduction in the serum levels of aminotransferases as a result of herbal administration during the present study might probably be due in part to the presence of isoflavones, polyphenols and other antioxidants as mentioned before which aided in reducing the liver injury induced by HFD.

For example, the water soluble antioxidant properties of phyllanthus was investigated by (Gazzani *et al.*, 2000) and evaluated in vitro and in ex vivo as protective activity against rat liver cell microsome lipid peroxidation.

Moreover, reduced fat cells in the liver as a result of reducing body weight may also improve liver function. In accordance with the present study, Zafar and Mujahid (1998); Mitra *et al.*, (2001) and Ahmed *et al.*, (2003) concluded that thymus and fennel has antihepatotoxic effect and significantly lowers serum levels of AST and ALT enzymes even in CCL4 intoxicated rats.

High fat fed animals showed significant increase in thyroid hormones when compared to normal diet fed animals. This result was agreed with Kuroshim *et al.*, (1971) who study the effects of a HFD for 4-5 weeks on thyroid activity and found that HFD caused a marked hypertrophy of brown and white adipose tissue, but no change in the weight of thyroid, while there was a significant decrease in the thyroid hormones. On the other hand, no available literature could be obtained concerning the effect of phyllanthus and thymus and fennel herbs on thyroid gland hormones but its effect on increasing thyroid hormones could be indirect result of their effect on lipids metabolism.

Our histopathological results showed that obese rats supplemented with mixture of thymus ,fennel and phyllanthus at 5,5 and 10% can prevent/reduce diet induce fatty liver. This fat reduction in the liver was confirmed by serum lipid analysis and by measurement of liver specific marker enzymes as mentioned before. Zafar and Mujahid (1998) and Ahmed *et al.*, (2003) reported that thymus, fennel and phyllanthus had antihepatotoxic activity and rats given it showed almost complete normalization of liver tissues, no fatty degeneration and no

necrosis. The observed improvements may be revealed to the presence of many antioxidant components found in herbs.

On the basis of the present results, we could conclude that herbal mixture of phyllanthus , thymus and fennel especially at 10,5 and 5% may have synergistic effect and its intake of be useful for treating obesity accompanied by hyperlipidemia as it reduces feed intake and body weight, improves serum lipid profile, liver function and thyroid activity in obese rats. Moreover, this mixture has a promising effect on the liver tissues as it ameliorates the histopathological lesions seen in this organ of obese rats.

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الدراسات البيولوجية والتشريحية المرضية على بعض خليط الأعشاب في الفئران السمينة

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الملخص العربى:

تم فى هذا البحث دراسة تأثير خليط الأعشاب بتركيزات مختلفة من مكونات الخليط (الزعتر، الشمر، الأملج) على بعض العوامل البيولوجية والنسيجية من الفئران السمينة. وتم توزيع ثلاثين من إناث الفئران البالغة إلى خمس مجموعات، أبقيت أول واحدة كمجموعة ضابطة سالبة، في حين غذيت المجموعات الأربع الأخرى على نظام غذائي عالي الدهون لاحداث السمنة. أبقيت واحدة من هذه المجموعات كمجموعة ضابطة موجبة, في حين أعطيت 4 مجموعات يوميا خليط من 20٪ من (الزعتر، الشمر والأملج) في (10 ، 5 ، 5٪) الخلطة الاولى، (10،5،5٪) الخلطة الثانية ، (5،5 ، 10٪) الخلطة الثالثة لمدة 4 أسابيع، وأظهرت النتائج أن الزيادة في وزن الجسم كان أقل بشكل ملحوظ خاصة في خليط من (الزعترو الشمر والأملج) (5،5 ، 10٪) مقارنة مع المجموعةالضابطه الموجبة و كما ان هذا الخليط خفض تركيزات الكوليسترول الكلي والدهون الثلاثية، LDL، VLDL وانخفض نشاط الانزيماتAST و ALT. وعلاوة على ذلك، تسبب في زيادة كبيرة في تركيز HDL- و تركيزات هرمون T3

وأظهر فحص الأنسجة حدوث تحسن في كبد الفئران السمينة التى تغذت على خليط من الأعشاب على مختلف المستويات. وتوصي هذه الدراسة أن تناول خليط من الزعتر، الشمر والأملج وخصوصا في (5،.5 ، 10٪) قد يكون من المفيد فى علاج السمنة.