Ministry of higher education
Babylon University
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Graduation Project

Experimental study of some drugs effects on the histology of liver

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بسم الله الرحمن الرحيم

نرفع درجات من نشاء

وفوق كل ذي علم

عليم

صدق الله العظيم

الاهداء

أهدي هذا البحث الى من قال الحق تعالى فيهما :

" وَقُل رَّبِّ ارْحَمْهُمَا كَمَا رَبَّيَانِي صَغِيرًا "

الى القلب الكبير والدي العظيم ..

الى والدتي العظيمة حفظها الله ورعاها برعايته ...

الى اخوتي والاصدقاء ومن كانو بصحبتي ومرافقتي اثناء دراستي

الى الاستاذ المشرف على هذا البحث د. فاخر مكطوف شمران ...

الى من انارو طريقنا ومستقبلنا بالنور (اساتذتي الاعزاء)

اهدي هذا الجهد المتواضع راجيه منهم القبول .

الشكر والتقدير

لابد لنا ونحن نخطو خطواتنا الاخيره في الحياه الجامعية من وقفه نعود الى اعوام قضيناها في رحاب الجامعه مع اساتذتنا الكرام الذين قدموا لنا الكثير باذلين بذلك جهودا كبيره في بناء جيل الغد .

وقبل ان نمضي نتقدم باسمى ايات الشكر والامتنان والتقدير والمحبة الى الذين حملو اقدس رساله في الحياه .....

الى الذين مهدوا طريق العلم والمعرفة ....

الى جميع اساتذتنا الافاضل .

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Introduction

OBISITY

Obesity is a complex, multifactorial disease that is strongly associated with multiple comorbidities [1-2]

These comorbidities include certain types of cancer, cardiovascular disease, disability, diabetes mellitus, gallbladder disease, hypertension, osteoarthritis, sleep apnea, and stroke. [1]

Obesity is associated with a high rate of cardiovascular andall-cause mortality [3]

Obesity results from an energy imbalance between caloric intake and caloric expenditure. Multiple factors, including genetics, socioeconomic status, environment, and individual decisions, all play a significant role in the pathogenesis of obesity. [3]

To understand obesity, a description of body weight classification for both adults and children is necessary. Body mass index (BMI) is the most widely used standard for classifying somatotype. BMI is obtained by dividing weight in kilograms by height in meters squared.

BMI classifications for white, Hispanic, and African American adults have been endorsed by the National Heart, Lung, and Blood Institute, the World Health Organization (WHO), the American Heart Association, American College of Cardiology, and The Obesity Society[5-4-2]

Normal weight: BMI greater than 18 to 24.9

kg/m2 Overweight: BMI greater than 25 to 29.9

kg/m2 Obesity: BMI greater than 30 kg/m2

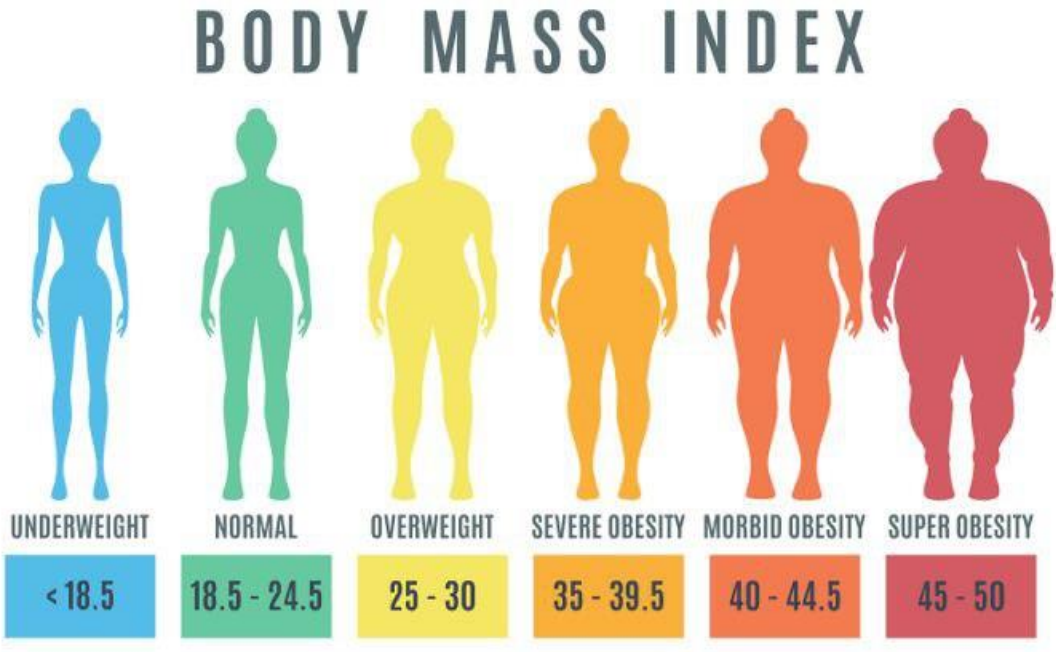
Obesity class I: BMI of 30 to 34.9

kg/m2Obesity class II: BMI of 35 to

39.9 kg/m2

Obesity class III (severe obesity): BMI greater than 40 kg/m2 (or>35 kg/m2 in the presence of comorbidities)

Body weight classifications also differ significantly between adults and children because of variations in growth and resultant body surface area. There are also significant differences between boys and girls.



Co-morbidities associated with obesity:

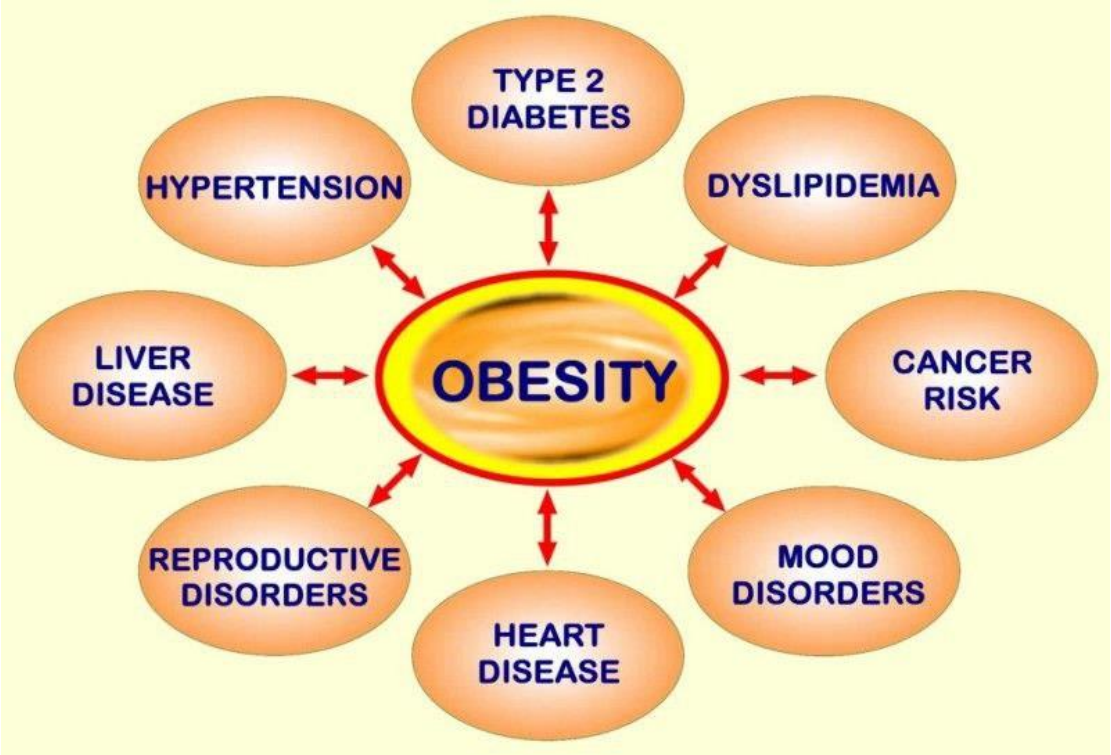
Obesity increases the risk of several physical and mental conditions. The co-morbidities are most commonly shown in metabolic syndrome, which includes: diabetes mellitus (type 2), high blood pressure, high blood cholesterol, and high triglyceride levels. [6]

_ The risk of obesity with higher co-morbidities are as follows :-

- *Cardiology* - ischemic heart disease, angina and myocardial infarction, congestive heart failure, high blood pressure, abnormal cholesterol levels, deep vein thrombosis and pulmonary embolism . [7]
- *Endocrinology* - Diabetes mellitus, polycystic ovarian syndrome, menstrual disorders, infertility, complications during pregnancy, birth defects and intrauterine fetal death. [7]
- *Psychiatry* - Depression in women and social stigmatization. [7]
- *Gastrointestinal* – Gastroesophageal reflux disease, fatty liver disease and cholelithiasis (gallstones). [7]
- *Neurology* - Stroke, neuralgia parenthetical, migraines, carpal tunnel syndrome, dementia, idiopathic intracranial hypertension and multiple sclerosis. [8]
- *Rheumatology and Orthopaedics* - Gout, poor mobility, osteoarthritis and low back pain. [9]

Today, obesity is a growing public health issue worldwide, with an increased risk for chronic and aggressive conditions such as respiratory complications, hypertension, diabetes mellitus, cardiovascular diseases, and cancer [11,12,13].

The increasing prevalence of overweight and obesity is seen in all age groups [12].



With the impact of obesity on health, quality of life, and social function, its management interventions are of great value [14].

Different management approaches are used to control and treat obesity, which are determined based on age, sex, puberty status, the severity of obesity, underlying causes, obesity-related complications, psychosocial factors, and patient and family preferences [15].

Due to fewer side effects, behavioral and dietary modifications and more exercise are considered the first-line treatment for weight loss in obese patients [16,17].

In addition, drug therapy is recommended for those whose lifestyle interventions alone are not responsive, especially if there is no possibility of bariatric surgery in these individuals [18].

The role of drugs in weight loss

The role of drugs in weight loss is controversial, and their effectiveness seems limited. It may be very effective for some people and not effective for others and may even have side effects for some [19, 20].

Phentermine is one of the oldest sympathomimetic drugs that contain diethylpropion. It is the most commonly used drug in the United States, accounting for 70% of prescriptions. The combination of **phentermine** and **topiramate** causes more weight loss than each of them separately [20].

Phentermine and ***topiramate*** extended-release (long-acting) capsules are used to help adults who are obese or who are overweight and have weight-related medical problems to loseweight and to keep from gaining back that weight [20].

Orlistat is a potent inhibitor of pancreatic lipase that reducesintestinal fat digestion [21].

Lorcaserin is a US food and drug administration (FDA)-approved selective agonist of the serotonin [5-hydroxytryptamine (5HT)]—2C receptor that is effective in weight loss by reducing appetite and increasing satiety [22].

This medication is used with a doctor-approved exercise, behavior change, and reduced-calorie diet program to help you lose weight, and taking orlistat can also help keep you from gaining back the weight you have lost [22].

Liraglutide, sold under the brand name Victoza, is an anti-diabetic

medication used to treat type 2 diabetes, obesity, and chronic weight management [23].

Liraglutide is used as a supplement to low-calorie diets and increased physical activity to control chronic overweight in adults [23].

Naltrexone/bupropion (contrave) combines an opioid receptor antagonist (naltrexone) with a dopamine and norepinephrine reuptake inhibitor (bupropion) in an extended-release tablet; the combination of naltrexone and bupropion reduces hunger and does not affect energy metabolism [23].

Pramlintide is an injectable drug that lowers the glucose level inthe blood, and it is used for treating type 1 and type 2 diabetes. Pramlintide is a synthetic hormone that resembles human amylin [21,22,23].

Lorcaserin, marketed under the brand name Belviq is a weight-loss drug developed by Arena Pharmaceuticals. It reduces appetite by activating a type of serotonin receptor known as the 5-HT2C receptor in a region of the brain called the hypothalamus, which is known to control appetite [21,22,23].

Several other drugs are used to treat obesity, but this systematicand network meta-analysis review focused on these mentioned drugs to determine which is the most effective drug in weight.

Lipo-6Black

is a potent fat burner that is formulated to destroyfat deposits.**It claims to** (24) **:**

- Boost your metabolic rate.

- Increase energy levels.

- Enhance mental alertness.

How Does Lipo-6 Black Work?

- This is a fat burner that boosts metabolism to allow the body toburn stubborn fat.
- It contains powerful ingredients that suppress appetite and allowyou to cut down on snacking between meals.
- Additionally, it boosts mental alertness and energy levels to keepyou going for long without fatigue. (25)

Here are some expected benefits:

- Increases metabolism.
- Boosts mental awareness keeping you sharp all day.
- Enhances energy levels.
- Reduce fat and carbohydrate absorption.
- Reduces cravings between meals. (24)

Ingredients of Lipo 6 are :

Caffeine 200 mg - Synephrine 20 mg - Guggulsterones 20 mg - Bioperine 5mg - Yohimbine 3mg.

- For instance, *coffee* may lead to jitters, headaches, nausea, and dizziness.

- *Yohimbine* may cause adverse effects, including high blood pressure, anxiety, gastrointestinal issues, and increased heart rate. Other severe conditions include seizures, acute kidney injury, and heart attack.

- *Vinpocetine* may cause the following side effects: immune suppression that may cause agranulocytosis (drop in white blood cells), stomach upsets, dry mouth, nausea, drowsiness, anxiety, headaches, facial flushing, and insomnia.

SIDE EEFECT OF LIPO 6

these products don't go through the same rigorous testing and FDA approval as prescription drugs

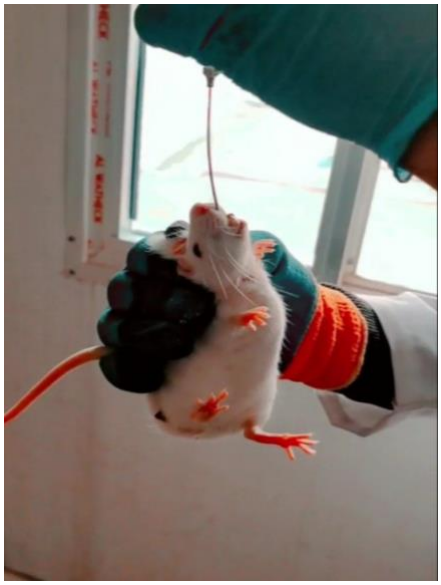
- It Can Cause a Caffeine Overload
- Nervousness
- Feeling jittery or shaky
- Nausea
- Vomiting
- Rapid heart rate
- Trouble sleeping
- In severe cases, seizures
- It May Lead to Heart Issues
- It Can Cause Digestive Problems
- It May Lead to Headaches (26_27)

Animals and breeding

Adult rats weighing between 170-200 g were employed in this experiment, with 15 animals total(5 controlled rats and 5 treated rats).The animals were placed into two groups at random, each with five animals. The animals were grown in the College of Pharmacy University of Babyloon animal home in plastic cages. The standard breeding conditions were 3 months with a laboratory temperature of 24±2oC. In addition to supplying the animals with adequate water and food during the duration of the experiment.

Chemical and Method

- Lipo 6 used in this experiment in form of powder
- In first trial we dissoved 0.5 mg lipo in 5cc DW and the rat can not tolerate this dose and 5 died
- In second trial we reduced the dose to 0.2mg in 5cc DW oral daily dose by intubation .
- The experiment last in rang in 3 month the rat weight reduced and then the rats anesthetized by use of ether and animals were sacrificed .
- In final step the liver collected for laboratory for histological analysis .



Results and discussion

The results of our study showed the presence of lymphocytes infelitration and vascular congestion as in the Figures ……

These results can be explained by the effects of caffeine which improved to have various deleterious effects .

Caffeine is metabolized by the microsomal P450 drug metabolizing enzymes, predominantly CYP 1A2.

Patients may have delayed metabolism of caffeine and experience caffeine side effects (nervousness, insomnia, headache) and increases in the antioxidant and tissue protectant glutathione at levels of intake that are well tolerated by patients without liver disease.

Energy drinks typically have high concentrations of caffeine but also a myriad of other components including vitamins, minerals, amino acids, sugar and various herbal products, the concentration and purity of which are usually unknown.

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لا تاتي الامور على قدر حليك

انما على قدر سعيك لها

Thank You