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Effect of Argel Herbs (*Solenostemma argel*) on-induced Liver Cirrhosis by Carbon Tetra Chloride in Rats

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Dedication

I would like to dedicate this work to my mother and the soul of my father for their support throughout my life .They provided me with lots and lots of tender and sacrifices.

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List of Abbreviations

ADA	**American Diabetic Association**
ALA	**A-linolenic Acid AA arachidonic acid**
ALD	**Alcoholic Liver Disease**
ALP	**Alkaline Phosphatase**
ALT	**Alanine Aminotransferase**
AST	**Aspartate Aminotransferase**
BMI	**Body Mass Index**
CAT	**Catalase**
CCl_4	**Carbon tetrachloride**
CVD	**Cardiovascular Disease**
DPPH	**1,2diphenyl-1-picryl hydrazyl**
Et-OH	**Ethanol**
FLD	**Fatty Liver Disease**
GAE	**Gallic Acid Equivalents**
GC-MS	**Gas Chromatography-Mass spectroscopy**
HPC	**Hepatocellular Carcinoma**
HDL-c	**High-density lipoprotein Cholesterol**
HDSD	**High-Digestible Starch Diet**
HF	**High Fat Diet**
HFD	**High fat diet**
HIAPP	**Human Islet Amyloid Polypeptide**
HMGA	**Hydroxy 3-Methyl Glutaric Acid**
HPLC	**High Performance Liquid Chromatography**
HRSD	**High-Resistant Starch Diet**
HSFD	**Highsaturated Fat Diet**
HUFD	**High-Unsaturated Fat Diet**
IR	**Infar-Red**
LCHF	**Low-Carbohydrate high-Fat**
LDL-c	**Low Density Lipoprotein Cholesterol**
MCDD	**Methionine Choline-Deficient Diet**
MCP	**Monocyte Chemotactic Protein**
MDA	**Malondialdehyde**
NAFLD	**Non-Alcoholic Fatty Liver Disease**
LPO	**Lipid Peroxidation**
PT	**Prothrombin Time**
PUFA	**Polyunsaturated Fatty Acids**
RDAs	**Recommended Dietary Allowances**
SDG	**Secoisolariciresinol Diglycoside**
SECO	**Secoisolariciresinol**
SOD	**Superoxide Dismutase**
SPI	**Sesame Protein Isolate**
T2DM	**Type 2 Diabetes Mellitus**
VEGF	**Vascular endothelial growth factor**
VLDL-C	**Very Low Density Lipoprotein-Cholesterol**

Abstract:-

Argel (*Solenostemma argel*) is a traditional edible herb that is commonly used in folkloric medicine for the treatment of rheumatic pain, inflammation, hyperlipidemia, hyperglycemia and antimicrobial agent due to its rich in bioactive component which act as antioxidants. Dried leaves Argel had a high content of carbohydrate and protein (76.19 and 14.10 g/100g on dry weight) respectively. Manganism were higher contents in Argel (98.40 mg/g) dry weight basis, repsctively than zinc and copper (4.40 and 10.0 mg/g, respectively).

Forty-eight male albino rats were used in biological experiments. Rats were fed the basal diet for two weeks prior to conducting the experiment. Initially, rats divided into six main groups and fed on rations for 42 days as follows: the negative control group (the first group) was fed on the basal diet. Forty male albino rats were fed on a basic diet and stimulated with carbon tetra chloride (CCl_4) in paraffin oil (50% v/v, 2 mL/Kg) twice a week by subcutaneous injection to induce chronic liver damage, then divided into 5 groups numbered from group 2 to group 6. Rats of the positive control group were fed basal diet until the final experiment. Group 3 and 4 rats were treated with dry leaves (0.5g and 1.0g, respectively) of Argel. Also, group 5 and 6 were fed on 50 ppm and 100 ppm of hydroethanolic extracts orally, respectively.

Biochemical analyses as serum ALT, AST, ALP and MDA were significant decreased in rats fed on dried and extracts in Argel compared to positive group. In Contrast, it could be that SOD activity in rat groups was significant increased compared to positive group. Also, Argel extracts had highest effect for liver parameters than dried Argel.

The best results of taste evaluation were in Kiwi pulp samples fortified with 50ppm and 100ppm argel water extract, then 50ppm, 100ppm argel ethanolic extracts, the values no significant difference between them (8.42, 7.50, 8.00 and 8.17, respectively) compared to control (8.42). At the same trend, results showed that no significant difference in odor (8.58, 8.83, 8.25, and 8.25, respectively) and color (8.92, 8.58, 8.25, and 8.83, repsictively) parameters in different groups.

These results are concluded that Argel could be suggested to the hepatoprotective effect of Argel may be due to its antioxidants content and free radical scavenging effect.

Keywords: Argel (*S. argel)*; Hydroethanolic extracts; Hepatoprotective; Oxidative stress.

1-Introduction:

Fat accumulation in the liver (hepatic steatosis) from nonalcoholic called Non-alcoholic fatty liver disease (NAFLD), this disease affects about 1.80 billion people **(Younossi et al., 2016).** In this respect, in **2009 Bellentani and Marino** reported that, 10-35% of the adult population in the worldwide suffering from NAFLD.

Cirrhosis is an increasing cause of morbidity and mortality in more developed countries, being the 14th most common cause of death worldwide but fourth in central Europe. Increasingly, cirrhosis has been seen to be not a single disease entity, but one that can be sub classified into distinct clinical prognostic stages, with 1-year mortality ranging from 1% to 57% depending on the stage. We review the current understanding of cirrhosis as a dynamic process and outline current therapeutic options for prevention and treatment of complications of cirrhosis, on the basis of the subclassifi cation in clinical stages. The new concept in management of patients with cirrhosis should be prevention and early intervention to stabilise disease progression and to avoid or delay clinical decompensation and the need for liver transplantation. The challenge in the 21st century is to prevent the need for liver transplantation in as many patients with cirrhosis as possible **(Tsochatzis et al., 2014)**.

Cirrhosis, or the generation of scar, is a dynamic process in chronic injury characterized by continuous accumulation of fibrosis ECM associated with concur-rent matrix degradation and remodeling. Like fibrosis disorders in other organs and tissues, fibrosis is a well- orchestrated wound-healing response. The response to chronic injury differs substantially from an acute tis-sue insult, in which there is no progressive scarring. From an evolutionary perspective, fibrosis is a log-ical response to tissue damage by encapsulating injury and maintaining tissue integrity for a sufficient time to enable the propagation of the species. However, over time, the fibrotic response impairs hepatic regeneration and shortens life expectancy, albeit in a time frame that no longer jeopardizes reproduction. In clinical terms, moderate tissue fibrosis is typically not associated with significant clinical signs or decreased organ function but is nonetheless an important determinant of prog-nosis over decades and sometimes in shorter intervals.

(Friedman and Pinzani, 2022).

Progressive fibrosis typically follows long-standing liver damage toxic drug-induced metabolic (NAFLD), cholesteric, or autoimmune insult. Eventually, fibrosis may lead to clinically evident cirrhosis and he-patic failure. Cirrhosis is defined as an advanced stage of fibrosis, characterized by the formation of regenerative nodules of liver parenchyma that are separated by, and encapsulated in, fibrotic septa. **(Pinzani and Macias-Barragan 2010)**

Argel is a desert plant commonly used in Egyptian and Sudanese traditional medicine to suppress appetite, for treatment of hyperglycemia, and hyperlipidemia and anti-inflammatory agent. The anti-diabetic, hypolipidemic and lipase inhibitory activities of Argel were reported in animal studies and *in-vitro* assays **(El-Shiek et al., 2019).**

Argel (*Solenostemma argel*) is widely distributed in Algeria, Libya, Mali, Sudan, Chad, Niger, Egypt, and Saudi Arabia. It has been reported to possess antimicrobial activity against pathogenic microorganism. Furthermore, this herb species has been used for treating rheumatic disease, loss of appetite, and cough **(Zain et al., 2012).** The curative properties of Argel include antispasmodic, purgative, antiulcerous, anti-inflammatory, and immunostimulatory properties **(Kamel et al., 2000 and Hamed et al., 2001).**

Argel known locally by the name (Hargel). It is indigenous to Africa. The parts used are the leaves and stems; the leaves contain high carbohydrates and protein as well as oil extract, and mineral as calcium and magnesium. The leaves are used in herbal medicine for the treatment of some illness as hepatic and renal and hypersentivities. It treats gastro-intestinal cramps, stomach-aches and urinary tract infections. Argel tea is used for lessening the pains of childbirth and for treating eating disorders since it increases appetite **(Murwan and El-Kheir, 2010).**

Argel is a medicinal plant with several therapeutic properties, and its leaves, bark, and stems are used in traditional medicine for the treatment of coughs, gastrointestinal cramps, urinary tract infections, rheumatic pains, diabetes, cardiovascular disorders, kidney, and liver diseases **(Al-Juhaimi, et al., 2018 a and b)**. The Argel leaves powder or extracts contains substantial quantities of a diverse range of phenolic compounds and possess antimicrobial and antioxidant activities **(Mohamed Ahmed et al., 2020).** Argel leaf powder and extracts have been used to improve the oxidative stability of camel patties **(Al-Juhaimi, et al., 2018 a)** and chicken **(Al-Juhaimi, et al., 2018 b).**

This plant is used in the treatment of hypercholesterolemia, diabetes mellitus, cold cough, jaundice and measles the plant also possesses insecticidal effect and hence was used to combat insect pests **(Awad et al., 2012)**. Moreover, it was reported to have antimicrobial properties as well as antibacterial and antioxidant activity **(Shafek and Michael, 2012)**. Most of Sudanese people in rural areas rely on traditional medicine for the treatment of many infectious diseases Argel, or locally called "Hargel" is an erect perennial under-shrub that reaches up to 1.5–2 feet in height with numerous branches carrying opposite decussate leaves. The leaves are lanceolate to oblong-ovate, with acute or sub–acute apex and cuneate base. The leaf petiole is thick.

Toxicological study conducted by **Shyoub et al., (2013)** to evaluate the acute toxicity of Argel and to determine the lethal doses of Argel in albino rats and local species of rabbits using intra-peritoneal doses. The results showed that the mean lethal dose was 6.35g/kg for the rabbits and 5.49g/kg for the rats. Another toxicological parameter determined was the median lethal dose (LD50) was 5.0 g/kg in albino rats.

Aims of the Study

Effect of Argel Herbs (*Solenostemma argel*) on-induced Liver Cirrhosis by Carbon Tetra Chloride in Rats

2-Review of Literature:-

2-1 Argel plant:

Medicinal plants are the most exclusive natural source of life saving drugs for the majority of the world's population. Compounds currently extracted from plants are used as pharmaceuticals, food additives, pigments, dyes, insecticides, cosmetics, perfumes and fine chemicals. Argel commonly growing in the Eastern Desert and along the Nile in South Egypt. It is a wild perennial shrub, with white flowers in auxiliary umbels, fruits ovate green-purple Argel leaves are used in Egyptian folk medicine as purgative, antipyretic, expectorant and as a remedy for bronchitis, for gastrointestinal cramps, stomach ache, colic, cold and urinary tract infections. In addition, this plant is used in herbal mixtures for the treatment of viral hepatitis B and C, as an immune-stimulant and for hypercholesterolemia**. Hegazi et al., (2006)** investigated the hepatotoxic and nephrotoxic effect of Argel. The plant also showed significant anti-cancer and anti-oxidant activities **(Hanafi and Mansour, 2011)**.

Also, medicinal plants are the main source of secondary metabolites, which are industrially important as they constitute pharmaceutically important herbs. As a result, there is a huge demand for these plants, which are overexploited from their natural habitat. Therefore, plant tissue culture is being potentially used as an alternative strategy for production of secondary metabolites. Flavonoids are important secondary metabolites having immense medicinal properties ranging from anti-oxidant, anti-cancerous, anti-inflammatory etc. To enhance the rapid and controlled, continuous production of this class of compounds, *in vitro* culture strategies application would ensure large scale and stable production throughout the year, under controlled environmental conditions. The present study is a stepping stone in *in vitro* production of the flavonoid kaempferol from callus cultures of Argel. Callus showed a potentiality for accumulation of kaempferol, especially from seedlings' stem **(Abd Alhady et al., 2016).**

Argel is a medicinal plant with several therapeutic properties, and its leaves, bark, and stems are used in traditional medicine for the treatment of coughs, gastrointestinal cramps, urinary tract infections, rheumatic pains, diabetes, cardiovascular disorders, kidney, and liver diseases **(Al-Juhaimi, et al., 2018 a and b)**. The Argel leaves powder or extracts contains substantial quantities of a diverse range of phenolic compounds and possess antimicrobial and antioxidant activities **(Al-Juhaimi et al., 2018a and b; Mohamed**

Ahmed et al., 2020). Argel leaf powder and extracts have been used to improve the oxidative stability of camel patties **(Al-Juhaimi, et al., 2018 a)** and chicken meatballs. Argel is a desert herb usually utilized in Egyptian and Sudanese traditional medicine to suppress appetite, for treatment of hyperglycemia, hyperlipidemia and anti-inflammatory agent. Previously, the anti-diabetic, hypolipidemic and lipase inhibitory activities of Argel were reported in animal studies and *in-vitro* assays **(El-Shiek et al., 2019).**

Argel is a wild herbal plant found in broad areas of Egypt, Saudi Arabia, and Sudan the leaves, bark, and stems of Argel have diverse medicinal applications and are traditionally being used for the treatment of numerous diseases such as pain, diabetes, respiratory tract infections, cardiovascular disorders, gastrointestinal problems, urinary tract infections, and kidney and liver diseases. Previous studies have shown that Argel leaves, bark and stems have antispasmodic, anti-inflammatory, ant nociceptive, antipyretic, anticancer, anti-oxidant and antimicrobial activities **(Awad et al., 2006)**.

Argel is a desert plant, widely spread in Central and North parts of Sudan, Egypt, Libya, Chad, Algeria, Saudi Arabia and Palestine. Moreover, Sudan is regarded as the richest source of Argel. Argel is widely extent in, Egypt, Sudan, Libya, Chad, Algeria, Saudi Arabia and Palestine **(Masoud and Li, 2015)**. This family is a gorgeous source of many important groups; indoline, alkaloids, steroids, pregnanes and their glycosides which possess antitumor and anticancer activities **(El-Sonbaty et al., 2016)**. Argel was described to alleviate gastrointestinal cramp, urinary tract infection and menstrual disturbance. Also, this plant has anti-bacterial, antifungal and antioxidant activity **(Farah and Ahmed, 2016)**.

The plant Argel known for their cardiac activity. Tamanrasset is situated in the South of Algeria, in the mountains of the Hoggar to 1400 m altitude. This city is in the heart of the Sahara, the biggest hot desert in the world. Argel is a Saharan species; it grows naturally in the Tassili n'Ajjer, in Tassili Hoggar, in the Tadrart. It is also widely distributed throughout North Africa (Egypt, Libya, Algeria and Sudan) and the Saudi Arabia **.**Leaves of this plant are used in indigenous medicine for the treatment of some diseases, such as the disease of liver and kidney. It is a powerful solution for bronchitis and is useful to treat neuralgia. It is utilized as incense in the treatment of measles and sometimes crushed and used as remedy for healing wounds. The leaves are useful to gastro-intestinal cramps and stomach colic **(Mohammed and Azhari, 2014).**