. **Republic of Iraq**

Ministry of Higher Education

Andscientific Research

University of Babylon

College of Pharmacy

The effect of the activity of Qurecus persica plant stem peel secondary compound extracts on Enterobius vermicularis parasite in vitro.

A graduation research submitted to the Babylon University Council, College of Pharmacy as part of the requirements for graduation and obtaining a Bachelor degree in Pharmacy (PhB degree)For the year 2023_2024

Done by :

Zainab Mohammad mahdi

Fatima ashour okab

Supervised By:

Rasha hadi Al-Issawi

Alaa hamady Al-taei

)الْعَالَمِينَ رَبِّ لِلَّهِ الْحَمْدُ أَنِ دَعْوَاهُمْ وَآخِرُ(

من العبد تخطى وما بفضله الا سعى ختم ولا جهد تم ما لله الحمد .... وجل عز الله من بفضل ومعونته الابتوفيقه وصعوبات عقبات

اللهم انفعني بما علمتني وانفع بي فالحمد لله على حسن التمام والختام

الاهداء

الى من يستحق الاهداء

إلى رفيق دربي و سندي ،الى ذالك الرجل العظيم الذي سعى جاهدا لتحقيق حلمي

الذي كان عوناً لي و سبب وقوفي هنا أبي الغالي

نور عيني ،الشمعة التي أضاءت دربي ،إلى من كان دعائها سر نجاحي امي الحبيبة

الي كل من ساندني ووقف معي خلال مسيرتي الدراسية

Acknowledgement

My Acknowledgement to Dr. Alaa Hammadi and Rasha hadi The supervisor of this research for her continuous assistance, patience with me and guidance, and she guided me in preparing the research plan and how to create a successful academic work. For completing this research,my Acknowledgement to the University of Babylon, College of Pharmacy and all its members. Thanks and appreciation to family and friends and everyone who contributed to the completion of this work..

The effect of the activity of *Qurecus persica* plant stem peel secondary compound extracts on *Enterobius vermicularis* parasite *in vitro*.

Abstract:

Q. persica plant stem peel found in north region of Iraq and has active compound and also used in traditional medicine in ancient time . This work was conduct to account the effects of cold and hot aqueous extracts

of *Q. persica* plant stem peel in paralysis and die of *E. vermicularis* parasite *in vitro* and determine the most influential plant for extracted secondary compound (alkaloid and phenolic compounds) from it to test in paralyze and kill of worms.

The stem peel of *Q. persica* plant was collect from Al-Heikma herbarium then the all extracts were prepared and experimented on this parasite, the results appear that cold aqueous extract of *Q. persica* plant stem peel have a high influential especially by 60 mg/ml concentration where its average arithmetic for paralysis and die of worms equal 143.66 ± 0.33 and 195.00 ± 0.57 minute , respectively, with clear significance differences, praziquantil drug successful through its high effect on parasite where its average arithmetic for paralysis and die of worms in 60 mg/ml concentration equal to 180.00±0.57 and 240.00± 0.57 i8 minute , respectively.

The results of secondary compounds of *Q. persica* plant stem peel appears that a high effects of phenolic compounds extract of *Q. persica* plant stem peel on paralysis and die of worms especially with 60 mg/ml concentration where its led to paralysis and die of worms at 80.00 ± 0.57 and 111.66 ± 0.88 minute , respectively, followed by alkaloid compounds that led to paralysis and die of worms with 60 mg/ml concentration at 211.00 ± 0.57and 203.00 ± 0.57 minute , respectively.

1-Introduction:

E. vermicularis (pinworm or threadworm) is considered as the most common intestinal parasitic worm infection of humans [1], it is a common parasitic infection spread throughout the world and usually causes infection in school going children, especially in rural areas and in poorer urban areas through the habit of fingers sucking [2] ,that present as peri-anal itching , attributed to the mucoid secretions of the eggs on the

skin [1] , this parasite is usually transmitted through close-contact between infected and uninfected persons, ingestion and inhalation of the eggs [3], also, reinfections one of the main causes of development of the infection, also it is spread by fecal-oral rout [4] . However, the complete life cycle of the helminth, from egg to adult worm, usually takes in 2 to 4 weeks [5].

E. vermicularis also causes or associated with chronic abdominal pain, urinary tract infection, salpingitis, eosinophilic ileocolitis , pelvic abscess ,inflammation of the anal or vaginal areas, intestinal irritation and difficulty sleeping [3,5].

Humans are the only natural host of *E.vermicularis*, which residing in the large intestine [6] , the diagnosis of *E. vermicularis* infection performs by microscopic examination of the characteristic worm eggs[7], sample collection by swabbing the anal folds using commercially available adhesive cellulose tape in the morning prior to defecation and before washing the genital area [8].

Praziquantel(PZQ), Albendazole and mebendazole are Benzimidazole carbamate derivatives which are regard as the preference drugs for *E. vermicularis* treatment [9], (PZQ) is a pyrazinoisoquinoline derivative [10],this pharmaceutical product is the first anthelminthic drug to fulfill the World Health Organization's requirements for population-based chemotherapy of a broad range of parasitic infections [11].

Although PZQ-effect on worms is very dramatic, the drug's precise mechanism of action on adult worms is unknown, most evidence implicates that tegument and muscles of susceptible parasites are targets of the action of praziquantel, within seconds of exposure to the drug[12], adult worm exhibit a rapid, sustained contraction of the worm's musculature [13], and vacuolization and disruption of the parasite tegument [14], Both of these responses are thought to be linked to a

praziquantel-dependent disruption of Ca2+ homeostasis [15]. The global protocol for treating *E. vermicularis* involves anthelmintic medication like mebendazole [4]. Treatment with mebendazole has shown efficacy in eradicating pinworms, as seen in cases of liver infection due to E. vermicularis [5,12].Iraqi protocol to treat *E. vermicularis* parasite: Albendazol cap 400 mg single dose Repeated after 14 days[5].

Currently , medicinal plants are used to treatment and remove diseases and the preservation of public health are widely globally spread (10) , where the humans have been using plants for their essential requirements such as food and medicine therefore the plants have been used in traditional medicine in order to cure and prevent various human disorders, [16], important advantage for therapeutic uses of the plants includes their safety, effectiveness, economic feasibility, and ease of availability [17].

Natural herbal products can fuse with drugs this are aimed to improve the effectiveness of medications because chemical drugs are more expensive and have several disadvantages , therefor herbal products reduce drug side effects [18]. Several naturally occurring compounds are potent antioxidants, both as free radical scavengers and as modulators of antioxidant enzymes expression and activity[19].

Species of the genus *Quercus persica* plant are important medicinal plants , over the centuries, these species have been used in folk medicine to treat various diseases [20]. *Quercus* species, also known as oak, represent an important genus of the Fagaceae family, It is widely distributed in temperate forests of the northern hemisphere and tropical climatic areas [21], many of its members have been used to treat and prevent various human disorders such as asthma, hemorrhoid, diarrhea, gastric ulcers and wound healing [20,21], it is has multiple biological

activities including anti-inflammatory, antibacterial, hepatoprotective, antidiabetic, anticancer, gastroprotective, antioxidant and cytotoxic activities, these effects attributed to the presence of bioactive compounds such as triterpenoids, phenolic acids and flavonoids [**22**].

Kurdistan of Iraq contain *Q. persica* oak which is widely distributed in it , also found in Turkey, Syria, Iraq , Persia, Cyprus, Greece [16] ,Herbal extracts have a high potential activity and low cellular toxicity, probably due to the activity of phenolic compounds, especially its tannin compounds, therefore, it will be a promising candidate to introduces a new agent without or with minimal cellular toxicity effect, the compound as tannins, flavonoids, and phenolic were found in *Q. persica* [17, 18].

The advantage of herbals materials return to their phenolic components and antioxidant capacities [18],which due to a high level amount of phenolic compounds, especially flavonoids and tannins in *Q. persica* extract which give it the potential effects as an antioxidant activity, Anti-virus antibacterial [19,20].

The alkaloids are substances of a very diverse class of plant secondary metabolites that have biological activities such as anticholinergic, antitumor, diuretic, antiviral, antihypertensive, antiulcer, analgesic, and anti-inflammatory [18], alkaloids are organic compounds containing cyclic nitrogen, such as: atropine, scopolamine and hyocsyamine [21], that are used in medicinal sides [22], contributed among toxins, neurotoxins and social drugs , alkaloids act primarily with the prevention of feeding and poisons for insects and other herbivores [23] , they act as catalysts for neural transport systems[24], different components as caffeine, nicotine, opiates and cocaine are consumed by humans [22,23].

Phenolic have one aromatic hydrocarbon ring containing one or more hydroxyl Groups of precursors phenylpropanoid pathway were attached , They range from simple components such as phenylpropanoids ,coumarin and benzoic acid to more complex components as tannins, stilbenes, and flavanoids [25], phenolics include components which represent toxicant materials for insects [26], phenolics have defense ability against bacterial or fungal attack and also have roles in the absorption of UV ray [25 , 26].The aim of this study is to evaluates the effect of active materials of *Q. persica* plant stem peel extracts on *E. vermicularis* parasite *in vitro*.

2-METHODS AND MATERIALS

2-1-plant materials Collect:

The stem peel of *Q. persica* plant were collected from the Al-Heikma herbarium at September 2023 , plant was diagnosed by the botanist in the plant department in the sciences college at the University of Babylon , Iraq . A sample of plant materials was grinding by electric grinder to get on an soft powder which kept in plastic plate and then save in the Herbarium lab. of the Pharmacognosy department , College of Pharmacy.

2-1-1-preparation of an cold aqueous extract for *Qurecus persica* plant :

Cold aqueous extract was attended by take 10 grams from the stem peel powder of the *Q. persica* plant and put it with 200 ml of distilled water in the flask 400 ml in size with using a mixer for 30 minute , then put in the test tube in the centrifuge for 10 minutes at 3000 rolls / minute, extract was dried by putting it in the oven at 45 C to obtain on dried extract , keep it in the fridge until use , hot aqueous extract for this plant was prepare by a same method but use boiling water [27] .

2-1-2-Extraction of secondary Plant component

2-1-2-1-Extraction of crude alkaloids :

10 g of dehydrated soft powder is extracted by putting it in the filter papers which fixed on thimbles , then adding 200 ml from ethanol alcohol (%99) for 24 hours by soxhlets apparatus . New products were concentrated with rotary evaporator apparatus. It dissolved in 5 ml of ethanol , with added 30 ml of Sulfuric acid (2%) , then using rotary evaporator apparatus to remove an ethanol alcohol . Mayer assay gives white product to ensure an present of alkaloids. Hydroxide ammonium (%10) was putting in separating funnel.

With putting (10) ml from chloroform, mixing of product was separating into two layers , selected the bottom layer because it contains alkaloids, it was concentrated with rotary evaporator , a new dry product kept in icebox [28] methods .

Figer(1) Separating funnel apparatus for alkaloids.

2-1-2-2-Extraction of crude phenolics:

Method of [29] was used to extracts phenolics, 20 gm of dried extract put in a glass flask with 400 ml of (%2) acetic acid by using the reflex condenser in (70) degree centigrade water bath for 8 hours . New suspension nominated and put it with N-propanol and sodium chloride substances in the Suppression of separation , been taking the top layer containing phenolic substances, then it was focused with evaporator rotor and dry product keeping in the fridge.

Figer(2) Separating funnel apparatus for phenolics.

2-2:Collection of *E. vermicularis* worm sample.

The adult worms were collected directly from an anus of children at midnight from Hilla center districts ,Babil Province ,Iraq. Then a worms washed with distal water and the parasites were kept in petridishes with phosphate buffer saline (PBS) in 37°C in incubator until the *in vitro* evaluation was started [30] .

2-2-1: Microscope assay:

The samples of helminths were collected from patients and diagnosed by light microscope using wet mount preparation for adult pinworms or eggs detection at microbiology Lab. Of laboratory and clinical department , pharmacy college, University of Babylon.

2-3:The Effects of plant extracts on *E. vermicularis* worm *In Vitro* .

Preparation of stock solutions of both extracts of the *Q. persica* plant stem peel which brings the melt (6) g of dry extract in (100) ml of distal water, therefore , stock solution become (60)mg/ml. Stock solutions are used for concentrations prepared (20,40 and 60)mg /ml, control is prepared from phosphate buffer saline(PBS) only .

The efficacy of both cold and hot water extracts were compared with praziquantel drug by the same concentrations. Four groups of worms , each group with five worms, one of them represented a control group , each group have been treated with an desired concentration of drug and extracts , the time for complete paralysis and death was recorded. External stimuli were applied as ascertain the paralysis time. The time

taken for worm become motionless was considered as paralysis time and lethal time was ascertained by death of motionless worm followed by fading of their body color [31] .

2-3-1: Testing the effectiveness of extracts:

The worms were assembled in petridishes which contain one ml of (PBS) then put in incubator ,after one hour, different concentrations of cold , hot and secondary compound extracts for *Q. persica* plant stem peel have been added to a petridishes that contain worm each on its own by adding one ml of each concentrations to a petridishes that contain parasite each on its own.In another petridishes that contain worm a same concentrations of praziquantil drug was added [32] .

2-3-3-The effects of Praziquantel drug on adult *Enterobius vermicularis* worm In Vitro

The stock solution of praziquantel drug was prepared by adding (600 mg) or one tablet of this drug after grinding into powder to 10 ml of distal water to become 60 mg/ml and a concentrations (20,40,60 mg/ml) were prepared in addition to control group, the time of paralysis and death was record with three replicates then taken one ml of each concentrations and added to a petridishes that included worm each on its own for praziquantel drug [32] .

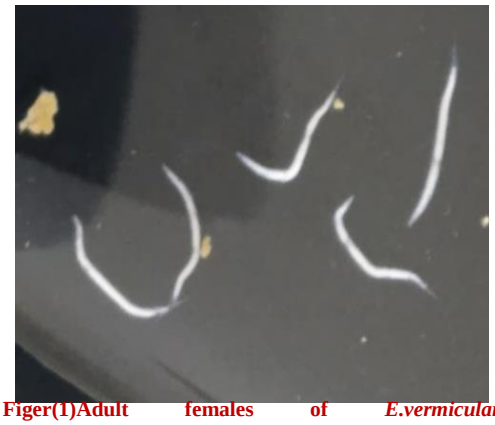
2-3-4:Estimation of pinworms worm Viability *In Vitro* .

The movement and death of worms has been monitored by looking, no movement or death of worm was identified [33] .

3-Statistical analysis:

Analyze of data take place by using factorial experiments with completely randomized (C.R.D)and using least significance differences at level (P<0.05) by using the statistics system (SPSS).

3-The results:



Figer(1)Adult females of *E.vermicularis*(10X).

Figer(2)Adult females of *E.vermicularis*(10X).

Figer(3)Ova with larvae of *E.vermicularis*(400X).

Figer(4)Adult females of *E.vermicularis*(10X).

Figer(4)Adult females of *E.vermicularis*(10X).

Table(1)The effect of extract concentrations overlapping for cold and

boiling aqueous extracts for *Qurecus persica* plant on worm paralysis and die *In Vitro*.

Qurecus persica plant	Extract type	concentration mg/ml	Time per minute for worm to paralysis	Time per minute for worm to die
			Mean±S.D.	Mean±S.D.
	Cold extract	60	143.66 ± 0.33	195.00 ± 0.57
		40	202.00 ± 0.57	243.00 ± 0.57
		20	220.00 ± 0.57	295.00 ± 0.57
		Control	1218.33 ± 32.37	1584.66 ± 2.84
	Hot extract	60	159.00 ± 0.57	213.00 ± 0.57
		40	190.00 ± 0.57	253.00 ± 0.57
		20	226.00 ± 0.57	282.66 ± 0.88
		Control	1239.33 ± 64.59	1592.00 ± 3.51
LSD at probality level 0.05			76.6	5.1

Table (2)The Interference Effect of Secondary Compound Concentrations for *Qurecus persica* plant on Worm Paralysis and Death *In vitro*.

Secondary compound type	concentration mg/ml	Time per minute for worm to paralysis Mean±S.D.	Time per minute for worm to die Mean±S.D.
Phenolics compounds	60	80.00 ± 0.57	111.66 ± 0.88
	40	100.00 ± 0.57	146.00 ± 0.57
	20	131.00 ± 0.57	189.00 ± 0.57
	Control	1252.66 ± 32.91	1563.66 ± 1.85
Alkaloids compounds	60	203.00 ± 0.57	211.00 ± 0.57
	40	331.00 ± 0.57	412.00 ± 0.57
	20	511.00 ± 0.57	641.00 ± 0.57
	Control	1259.00 ± 30.00	1577.33 ± 6.06
LSD at probality level 0.05		47.2	7

Table (3) The effect of Praziquantel drug on worm paralysis and die *In Vitro*.

Concentration of drug (mg/ml)	Time per minute for paralysis Mean ± S.D	Time per minute for die Mean ± S.D
60	180.00±0.57	240.00± 0.57
40	201.00±0.88	275.66±0.33
20	328.00±2.51	442.00±0.57
Control	1252.66±40.95	1562.00±2.30
LSD at probality level 0.05	67	4

5-Discussion:

E. vermicularis (Nematoda), a pinworm, is a global helminthic parasite of humans that is especially common in temperate climates [3]. Medicinal plants represent the most ancient form of medication, used for thousands of years in traditional medicine in many countries around the world [34], it's treating and preventing various diseases [35].

The results of this study demonstrate a high affectivity for a cold water comparative with a boiling water of *Q. persica* plant extract on a paralysis and die of *E. vermicularis* helminths,this finding appears that a cold water of *Q. persica* plant extract was very active and have ability to destroy or killed a worm and this is effect may be that a cold water extract contain active substances that effect on neuromuscular system and led to die this a ability may be because of an extract contain many active components in the fruit includes flavonoids and also other compounds such as a phenolic acids, coumarins, carboxylic acids, aminoacids and vitamins [36] ,or may be because it's a rich with phenolic (acids ferulic acid, synapic acid) that alters a PH media of worm and leads to kills it,or a phenolic compound adhere with tegument cells of helminths and stopped it's activity , where a phenolic compounds are dissolve in water [37] , or an activity of *Q. persica* plant a cold water extract may be due to that active components or substances high decomposes in cold water that lead to concentration of this substance that effect on parasite more than in boiling water because a hot may be broke or damage an effective substances in plant that lead to reduces its activity on worms .

Therapeutic effects of *Q persica* plant arising from consuming bioactive components including providence energy, regulation of cell metabolism, immunoregulation, antioxidation, anticoagulation [38],differential *Q. persica* plant varieties having different impact on human health as well as body metabolism [39] . *Q. persica* plant had greater activity than other simple disinfectant material [40] , *Q. persica*

plant act as medicinal and therapeutic potential advantages as anti-carcinogenic, anti-glycemic, anti-cardiovascular , antioxidant , antimicrobial [41].

From this study we conclude that a best water extract that lead to a paralysis and die of *E. vermicularis* helminths in short period time was cold aqueous extract *of Q. persica* plant more than hot extract.

This part of the study aims to find out the impact of an effectiveness of secondary compounds in paralysis and die of worm where this study proven that phenolics compound of *Q. persica* plant are more influential than the alkaloid compounds it led to worm paralysis and death in a short period of time, where was a time for a worm to paralysis was (80.00 ± 0.57) minute and for worm to die was (111.66 ± 0.88) minute, this finding appears that phenolics compound of *Q. persica* plant may be effect by because of the ability of these phenolic compounds to object respiratory process in mitochondria, then inhibition of carbohydrates, fats and intermediate the reactions of metabolism of proteins which are important for worm viability or because of the ability of chemical compounds to destruct the cell membrane contain in fats and proteins (39), therefore the process leads to death of worm parasite (38,40) , other studies appeared that phenolic extract inhibits respiratory chain enzymes including thiol group (-SH) which is replaced by the carbonyl group existent in phenolics after oxidation of hydroxyl group (-OH) by molecular O and removal of a hydrogen molecule (42).There are many vital activities for phenolics which have some curative properties such as anti-inflammatory, anticancer, antiviral ,antibacterial and antioxidant activities (43), this effect of phenolic compounds probably attributed to its rich with tannins [44] ,tannin affects protein composition in worms exposed to high concentrations and thus affecting the neural receptors which leads to the

worm's paralysis and death [45], tannins polyphenols binding to protein through hydrogen bonds and forming a tannin–protein complex [46] ,or tannins destroys an organism's cell membrane through its effect on the fats and proteins in it and then the organism loses its ability to grow or penetrates a cell membranes and obscures the active sites of some enzymes inside the cell which is necessary for growth [47] . Phenolic compounds are recognized as being responsible for an antioxidant and antihelminthic ability [48].

The results of this study appear that alkaloids compounds have antihelminthic activity on paralysis and die of *E. vermicularis* helminths, this activity of alkaloids compounds as follow where was a time for a worm to paralysis

was (203.00 ± 0.57) minute and for worm to die was (211.00 ± 0.57) minute, these finding can be attributed to that alkaloids may be disrupting the action of the enzyme, receptors and proteins by forming hydrogen bonds with this compound where they have functional groups, a proton accepting nitrogen atom, and one or even more proton donating amine hydrogen atoms [49] ,such as pergularinine and tylophorinidine alkaloids both of them inhibit the activity of dihydrofolate reductase that are responsible for nucleic acid synthesis [50] ,or an alkaloids may be binds to protein that important in cell division with high affinity causing inhibition of proteins and its enzyme activity which led to inhibition of cell division [51] ,or an alkaloid may be acts through a detergent-like mechanism that led to disruption of outer membrane of microorganisms [52] , also an activity of alkaloids may be attributed to inhibition of virulence factors of microorganisms [53] . Alkaloids have many pharmacological properties, such as central nervous system stimulants , anticholinergic agents oxytocic and vasoconstrictor activity ,anti-inflammatory and antimalarial activity [54] ,the anti-inflammatory activity of alkaloids, involving inhibition or regulation of important inflammation mediators [55].

The static analysis for findings of interference effects of praziquantil drug concentrations demonstrated that praziquantil drug possess a high activity on a paralysis and die of *E. vermicularis* helminths especially with 60 mg\ml where was a time for a worm to paralysis was (180.00±0.57) minute and for worm to die was (240.00± 0.57) minute, this finding agree with the finding of (56,57) each of them proved that praziquantil drug has a high activity against the helminths as (56),Where the (56) They were evaluated the activity of PZQ on *Schistosoma haematobium* , inhibition concentration (IC50) values on adult *S. haematobium* were determined in vitro, their results appeared or

displayed the highest activity against adult worms in vitro, revealing that IC50 of 0.007 μg/ml at 4 h and 0.01 μg/ml at 72 h, as well as the (57)they were performance this study to compare the efficacy of a herbal drug as Schitozim over praziquantel in the management of *Schistosoma. mansoni* infection in BALB/c mice and through they performed the three infected group, two of it treated with the praziquantel (25 mg/kg, or 50 mg/kg) while the third group was untreated, the results appeared that the drug made significantly reduced in the adult-worm burdens .

The effect of praziquantel drug in this research probably due to that praziquantel is effects on the beta subunits of voltage-gated Ca2+ channels which identified as potential molecular targets of praziquantel [58], where the rapid influx of calcium ion (Ca2+) lead to morphological changes of the worm, which include rapid contraction of the musculature and tegumental bleb and vacuole formation in the tegument and tegumental damage [59], or the praziquantel drug is blocking of the adenosine receptors of the worms by praziquantel, causing calcium influx in the drug's activity [60 ; 58].

Praziquantel is a broad-spectrum, highly efficacious and safe, anthelmintic against trematode and cestode infections in humans and animals (61).Praziquantel (PZQ) is the mainstay and responsible for the activity of parasitic worm control and has been successfully used for decades (56).Praziquantel is an essential drug for treating parasitic infections like schistosomiasis, [61]. It activates a transient receptor potential elastatin ion channel in worms, causing Ca2+ entry and paralysis [58].

Conclusion

• The cold water extract of *Q persica* plant has a high effect on paralysis and die of *E. vermicularis* worm more than boiling water extract In *Vitro.*

• The phenolic compounds of *Q. persica* plant with (60 mg/ml) has a high efficient on paralysis and die of *E. vermicularis* worm, then alkaloid compound .

Acknowledgements

We introduce acknowledgements for handling people in the Pharmacognosy laboratory for helping us in search completion .

References:

[1] Gosttein, B (1992) . Molecular and immunological diagnosis of *E. vermicularis*. Clin . Microbial. Ref .,5:248-261.

[2] Al-dabk ,Muhmmed Abdulla and Al-Janabi, Talal Aboud (1990). *E. vermicularis* , 1st Pup , Al-Etedal Comp. Baghdad.

[3] Doty, J.E., Tompkins, R.K. (1989)."management of enterobiasis disease . Surg. Cli. North Am.; 69:285-95.

[4] Safioleas M, Misiakos EP, Kaisis J, " treatment of human enterobiasis " Int. Surg. 2000; 85:358-65.

[5] Al-aubaidi.T. E. (2010). Treatment of enterobiasis. The Iraqi post. Medi .J. V.(9), N.(2),p:189-195.

[6] Thompson ,R.C., McManus, D.P.,"Etiology: parasite and life cycle "in: Eckert J, Gemmell, M.A., Meslin, F.X.,eds. Manual on enterobiasis in humans: A public health problem of global concern. WHO\O\E 2001: 1-19.

[7] Langer, J.C., Rose, D.B., Keystone, J.S. " diagnosis and management of enterobiasis " Ann. Surg. 1984; 199:412-17.

[8] Gomez MA, Craxatto JO, Cravetto L, Ebner R. enterobiasis of the orbit. A review of 35 cases. Ophthalmology; 1988; 8:1027-32.

[9] Edan ,E. M. and Ardalan ,N. M. Estimation of humeral immune response that immunizing with enterobiasis antigens by using IHAT and Elisa. *2009* Fac. Med. Baghdad, 2009; Vol. 51, No.3.

[10] Veiga Junior VF, Pinto AC, Maciel MAM. Plantas medicinais: cura segura? Quim Nova. 2005;28:519–528.

[11] Arun, M., Asha, V.V. (2008).Gastroprotective effect of Dodonaea viscosa on various experimental ulcer models. J. Ethnopharmacol. ;118:460–465.

[12] Reuter S, Buck A, Grebe O, Nüssle-Kügele K, Kern P, Manfras BJ. Salvage treatment with amphotericin B in progressive human alveolar enterobiasis. Antimicrob Agents Chemother 2003; 47: 3586-3591.

[13] Deger E, Hokelek M, Deger BA, Tutar E, Asil M, Pakdemirli E. A new therapeutic approach for the treatment of cystic enterobiasis. Am J Gastroenterol 2000; 95: 248-254.

[14] Villarreal EC. Current and potential therapies for the treatment of herpes virus infections. Prog Drug Res. 2003;60:263–307. [PubMed]

[15] Panahi P, Jamzad Z, Pourmajidian MR, Fallah A, Pourhashemi M, Sohrabi H. Taxonomic revision of the Quercus brantii complex (Fagaceae) in Iran with emphasis on leaf and pollen micromorphology. Acta Bot. Hung. 2012;54:355–375.

[16] Evans ,W. C., *Trease and Evans Pharmacognosy*, Elsevier, Uttar Pradesh, 15th edition, 2009.

[17] Karimi, A. [1] Mohammad-Taghi Moradi,[1] Mojtaba Saeedi,[1] Sedigheh Asgari and Mahmoud Rafieian-kopaei[1]2013; Antiviral activity of *Quercus persica* L.: High efficacy and low toxicityAdv Biomed Res. 2: 36.

[18] Rabindran R, Muthulakshmi P, Ganapathy T, Doraiswamy S. Induction of resistance in rice to rice Tungro Virus using horsegram (Vigna unguiculata Walp. Sub sp. unguiculata) seed sprout extract Madras Agric J. 2003;90:286–8.

[19] Muliawan Y, Shamala SY, Devi LS, Hashim O, Yusof R. Inhibitory potential of Quercus lusitanica extract on Dengue Virus type 2 replication. Southeast Asian J Trop Med Public Health. 2006;37:132–5.

[20] Chang C, Yang M, Wen H, Chern J. Estimation of total flavonoid content in propolis by two complementary colorimetric methods. J Food Drug Anal. 2002;10:178–82.

[21] Zulak K, Liscombe D, Ashihara H, Facchini P. Alkaloids. Plant secondary metabolism in diet and human health. Oxford: Blackwell Publishing; 2006. p. 102–36.

[22] Goldman P. Herbal medicines today and the roots of modern pharmacology. Ann Intern Med. 2001;135:594–600.

[23] Harborne J. R. Introduction to ecological biochemistry. 4th ed. London: Elsevier; 1993.

[24] Wink M. Interference of alkaloids with neuroreceptors and ion channels. Stud Nat Prod Chem. 2000;21:3–122.

[25] Zenk MH, Juenger M. Evolution and current status of the photochemistry of nitrogenous compounds. Photochemistry. 2007;68:2757–72.

[26] David O. Kennedy and Emma L. Wightman (2011) . Herbal Extracts and Phytochemicals: Plant Secondary Metabolites and the Enhancement of Human Brain Function1. Adv. Nutr. 2: 32–50.

[27] Diaz Napal GN, Defago MT, Valladares GR, Palacios SM. Response of Epilachna paenulata to two flavonoids, pinocembrin and quercetin, in a comparative study. J Chem Ecol. 2010;36:898–904.

[28] Treutter D. Significance of flavonoids in plant resistance: a review. Environ Chem Lett. 2006;4:147–57.

[29] Hernandez,M. ;Lopez, R. ; Abanas,R.M. ;Paris, V. and Arias, A. (1994).Antimicrobial activity of Visneamocanera Leaf extract. J.Ethnopharmacology., 41 :115-119.

[30] Al-Samaraei, K. W. (1983). Distribution of alkaloids and its taxonomic significance in some wild species of the family Solanaceae in Iraq. Master's thesis, college of Science, University of Baghdad: 157 pp.

[31] Ribereaun Gayon , P.(1972). Plant phenolics . Oliver and boyd. U.S.A. 254 pp.

[32] Smyth ,J.D.,(1985). In vitro culture of enterobiasis Spp. In : Proceedings of the 13th. Int. Congr. Madrid,1985,pp.,84- 89.

[33] Kadir M, Rasheed S, Tahir S. Comparison between the efficacy of some chemical drugs and medical herbs on some parasite. In Abstracts of the 11th Sci Cong Fac. Vet. Med., Assiut Univ., Egypt. 2004, p 372-382.

[34] Smyth JD and Barrett NJ. Procedures for testing the viability of some worm. Trans R Soc Trop Med Hyg 1980; 74: 849-852

[35] Doaa A. Yones1,*, Gamal A. Taher2 and Zedan Z. Ibraheim3 .(*2011).*In Vitro Effects of Some Herbs Used in Egyptian Traditional Medicine on earth worm, Korean J. Parasitol Vol. 49, No. 3: 255-263.

[36] Nepalia ,S., Joshi, A., Shende, A., Sharma, S.S. (2006). Management of enterobiasis . Department of Gastroenterology , SMS Medical College and Hospital , Jai Pur . JAPI. p. 54.

[37] Fadhil, A. A. and Baiee, H. A.(2018). Epidemiological and Clinical Features of enterobiasis in Babylon Province, During the years 2010-2015. Bab. Uni. J./ Pure and Applied Sciences/ No.(2)/ Vol.(26).

[38] Rassan AF. A study on possibility of the attenuation of enterobiasis by using various drugs. M.Sc. thesis. College of Medicine, Baghdad University,. 1994.

[39] Zhang, W.; Li, J. and McManus, D.P.(2003) Concepts in immunology and diagnosis of enterobiasis. Clin Microbiol Rev; 16: 18-36.

[40] Khalaf ,A. K.H. ; Al- Mayah, S. H. and Athbi ,A. , M. (2011). In vitro activity of alkaloids extraction from chlorophyta and cyanophyta against the earth worm. Thi-Qar Med. J. (TQMJ): V.(5) N.(3): (56-70).

[41] AL-Quraishi1, M. A. ; Shaalan, N. N. and Almusawi ,H.S .(2015).Study the effect of *Artemisia* Herba-alba extracts in adult and larval stages of *Echinococcus granulosus* parasite in vivo and in vitro. Int.J.Curr.Microbiol.App.Sci. 4(8): 267-282.

[42] John , D. T. and Petri , W. A. (2006) . Markell and Voge's medical parasitology . 9th edn . Elsevier , Inc . USA . 224-231.

[43] Ma , X. M. ; Bao , G. SH. , Wan , J. M. ; Liao, D. J. ; Yin , SH. F. ; Meng , X. Q. ; Zhou, G. K. ; Lu, X. M. and Li, H. Y. (2007). Therapeutic

effect of *Sophora moorcrofliana* alkaloids in combination with albendazole in mice experimentally infected with protoscolices of *Echinococcus granulosus* . Braz. J. Med. Biol. Res. , 40(10):1463-1708.

[44] Rafiei, A. ; Pipelzadeh ,M. H.; Jahanshahi , A.; Erfanian , Salim, M. R. (2009). Comparing the effectiveness of albendazole and combination of albendazole and praziquantel in experimental hydatidosis. Iranian Journal of Clinical Infectious Diseases;4(1):9-12.

[45] Pawlowski, Z.S. (1997) Critical points in the clinical management of enterobiasis: Arevised review. In: Andersen FL, Ouhelli H, Kachani M (eds), Compendium on cystic echinococcosis in Africa and in Middle Eastern countries with special reference to Morocco. Brigham Young University Print Services, Provo, 119-135.

[46] Topcu O, Aydin C, Arici S, Duman M, Koyuncu A, Sen M. The effects of various agents on the hepatopancreatic biliary system. Viszeralmedizin. 2006;22:185–190.

[47] Gholami SH, Rahimi-Esboei B, Ebrahimzadeh MA, Pourhajibagher M. In vitro effect of *Sambucus ebulus*on on enterobiasis in vivo. Eur Rev Med Pharmacol Sci. 2013;17:1760–1765.

[48] Mahmoudvand, H.;Nadri ,S; Rezaeifar , M. and Rezaeifar ,M. (2016).Scolicidal effects of Myrtle methanolic extract on hydatid cyst protoscolices with praziquantil . Der Pharmacia Lettre, , 8 (8):19-22

[49] Larki, S. 1; Jalali , M. H. R.,1 and Goodarzi, S. (2017). Effects of Gallic Acid, One of the Major Compounds of Plants, on enterobiasis **in vivo .** Zahedan J. Res. Med. Sci. May; 19(5):e9791.

[50] Baidez AG, Gomez P, Del Rio JA, Ortuno A. Dysfunctionality of the xylem in Olea europaea L. Plants associated with the infection process by Verticillium dahliae Kleb. Role of phenolic compounds in

plant defense mechanism. *J Agric Food Chem.* 2007;**55**(9):3373–7. doi: 10.1021/jf063166d. [PubMed: 17394331].

[51]. Han X, Shen T, Lou H. Dietary Polyphenols and Their Biological Significance. *Int J Mol Sci.* 2007;**8**(9):950–88. doi: 10.3390/i8090950.

[52] Veeriah S, Kautenburger T, Habermann N, Sauer J, Dietrich H, Will F, et al. Apple flavonoids inhibit growth of HT29 human colon cancer cells and modulate expression of genes involved in the biotransformation of xenobiotics. *Mol Carcinog.* 2006;**45**(3):164–74. doi: 10.1002/mc.20158. [PubMed: 16369997].

[53] Owen RW, Giacosa A, Hull WE, Haubner R, Spiegelhalder B, Bartsch H. The antioxidant/anticancer potential of phenolic compounds isolated from olive oil. *Eur J Cancer.* 2000;**36**(10):1235–47. [PubMed: 10882862].

[54] Houghton, P.J.; Zarks, R. ; De-les- Heras, B. and Hoult,J.R.(1995). Fixed oil of Nigella sativa and dried thymoquinine inhibit aeicosanoid generation in Leukocyte and membrane lipid ., Peroxidation . Med. Planta, 61(1): 33 –36.

[55] Hailat, N.; Al-Kahil, S.; Al-Kohi , A.; Lafi, S.; Al-Anif; Al - Darragii, A. and Batainch, Z. (1998) . Effect of Nigella sativa extracts on antibody response of rats vaccinated with Brucella vaccine. (Rev. 1), Pharmaceutical Biology. , 36 (3): 217 – 221 .

[56] Kovac ,J. ; Vargas, M.; and Keiser, J. (2017) .In vitro and in vivo activity of R- and S- praziquantel enantiomers and the main human metabolite trans-4-hydroxypraziquantel against *Schistosoma haematobium*. Parasites & Vectors,J. 10:365.

[57]Lamberton, P.H.L., Faust, C.L. and Webster, J. P. (2017). Praziquantel decreases fecundity in Schistosoma mansoni adult worms that survive treatment: evidence from a laboratory life-history trade-offs selection Study . Infectious Diseases of Poverty, J. 6:110

[58] Brunton, L. L. and Knollmann ,B. C.(2022). Goodman and Gilman's the pharmacological basis of therapeutic. 14th edition. Mc Graw Hill publisher. Page 1334.

[59] Chan, J.D; Zarowiecki, M.; Marchant, J.S .(2012). Ca(2+) channels and Praziquantel: A view from the free world. Parasitol Int;pii:S1383-5769.

[60] Doenhoff, MJ, Cioli D, Utzinger J. Praziquantel: mechanisms of action, resistance and new derivatives for schistosomiasis. Curr Opin Infect Dis 2008;21:659-67.

[61] Chai, J.-Y. (2013). Praziquantel Treatment in Trematode and Cestode Infections: An Update review Article, J. of Infect Chemother:45(1):32-43.