Antiagnostic Effect of Musk and Sidr Leaves on Some of the Opportunistic Fungi that Cause Lung Toxicity

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Abstract: Opportunistic fungi play a great role in causing some of the dangerous diseases affecting human and animal. In this study five types of those Fungi were used for the experimental study. Those to the following five groups: *Aspergillus flavus, Aspergillus fumigates, Rhizopus stolonifer, Fusarium solani* and *Candida albicans.* That was done to study the effect of natural musk and sidr plant leaves and extracts to inhibition the growth of Fungi. The results showed significant data in inhibition of Fungi *A. flavus* and *A. fumigates*.The percentage of suppression reached 74.61% and 68.76% while The percentage of suppression in fungi, *R. stolonifer* and *F. solani* were 67.80% and 71.75%. Besides their effects on fungus *C. albicans* in the percentage of 56.92%. The results were confirmed and in agreement with the histological examination of the infected rat lung due to inter peritoneal injection with suspension of *A. flavus* after treatment with musk and sidr extracts twice weekly for 30 days by a dose equals 0.02kg/body weight. Then compared with normal control rats. rats were divided into two groups: the first control group was subdivision groups was injected with a- distilled water. b- suspention fungus *A. flavus*. c- musk extract. d -sidr extract. e- both musk and sidr extracts. The second experimental group was subdivided was injected with: a- suspension of pathogenic fungus *A. flavus* and musk extract. b-suspension of pathogenic fungus *A. flavus* and sidr extract. c- suspension of pathogenic fungus *A. flavus* and of both musk and sidr extracts. Histological study showed decrease in toxicity of the fungus (*A. flavus*) on the rat lungs after treatment with musk and sidr.These results indicated that musk and sidr can be used as safe natural product in management and control of lung toxicity (that is one of the manifestat of lung cancer) instead of drug chemotherapy.
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Key words: The Opportunistic Fungi, Musk, Sidr, Lung

1.Introduction:

Opportunistic fungi are present all around in the environment, they are found in the following main groups: *Aspergillus*, *Mucor*, *Rhizopus* and *Candida*. Most susceptible persons are those who were under treatment with broad-spectrum antibiotic or the immune suppression drugs. The fungi can cause severe diseases although they are non pathogenic fungi initially.

Fungi can cause Aspergillosis, pneumomycosis or bronchomycosis. Long time exposures to decorating plants in houses or hospitals can cause lung infection that simulates tuberculosis. The most common fungus causesing diseases is *Aspergillus fumigatus*, however, other species can cause diseases such as *Aspergillus flavus, Aspergillus niger* and *Aspergillus terreus*. Clinical signs of Aspergillus infection can be classify into three types: Allergic Aspergillosis, with similar symptoms to bronchial asthma disease. It can be dangerous and chronic associated with broncho constriction. Colonizing Aspergillosis is characterized by formation of Aspergilloma (mycotic swelling) caused due to condensation and accumulation of mycotic filaments of fungal growth that occupied lung surface, clinical signs of the disease are similar to what occurs in severe allergy but it is associated with hemoptysis. The third is the infection with the invasive Aspergillosis. Filaments of the pathogenic fungus invade tissues locally or by spreading and can cause respiratory infection after fungal colonization ot the bronchi and bronchioles causing bronchopneumonia. Mycotic filament when invading blood vessel Lumina causes pulmonary hemorrhage, infection included nose, and nasal sinuses (Al- Bawab., 1993). *Fusarium solani* is one of the opportunistic fungi, its toxicity is known by Fusariotoxicosis caused by mold corn toxicosis in many animals. Besides the harm occurs due to *Fusariom* infection that can cause stem rottining of *Zea mays* and necrosis, as well as scrab of barley and wheat. Makun *et al.,* (2007) found that among 49 millet there were 12 of them infected by Aflatoxin B_1 and 35 out of 55 of isolated fungi to study their toxin production are considered a rat killer were *Fusarium*, *Aspergillus*, *Penicillium*, *Mucor, and Rhizopus*. Lungs toxicity occurs due to fungal infection by *Fusarium solani* due to toxin production such as Ipomearon and some other metabolic furanoid products that causes pneumonia (Abd El-Hamied., 2000).

Moreover, infection by yeast *Candida albicans* causes dangerous hazards on heart, spinal cord, urinary tract and causes damages when they occupy lungs (Toma *et al*., 2008). As for contamination by

Mucor and *Rhizopus*, infection can affect persons suffering from metabolic disorders such as Diabetes leading to high mortality rate (Al- Bawab., 1993).

Repeated consuption of antibiotics lead to development of more resistant fungi and increased damages of great amount of disease spread with side effects. Hsueh *et al*., (2005) mentioned that among 59 isolated spore species from *C. glabrata* about 16 appeared isolated (27%), and were not affected by the antifungal fluconazole. So, most researches were directed and dedicated to study and discover new natural sources that can suppress pathogenic fungi and replace chemical use of the antifungal drug. One of those sources was the natural musk, Saddiq., (2007) mentioned that 25% of musk gave the highest percentage of suppression of bio mass for each of *A. niger*, *F. oxysporum* and *C. albicans*. The percentage for dry weight reached 16.86%, 17.2% and 4,2% respectively comparing with control samples. As mentioned by Ali *et al*., (2001) and Suksmrarn *et al*., (2006) and sidr can be used as natural source in suppression of gram positive bacteria, and in management of some wounds and skin diseases as well as its action as anti pyretic (Shahat *et al*., 2001).

Adzu *et al*., (2002) explained the palliative effect of sidr extract on rats treated with 100 – 200 mg/kg body weight by oral administration that was expressed in the form of increased sleep periods and decreased spontaneous motor activity (SMA) of the treated rats. Saddiq and Al-Elyani (2009) mentioned the high potency of both musk and sidr in limiting liver toxicity in rats treated with *Aspergillus flavus* and Aaflatoxin. The research aimed to study the effect of musk and sidr leaves and their extracts on the growth of five types of pathogenic opportunistic fungi representing the major fungal groups. The experimental fungi are *Aspergillus flavus*, *Aspergillus fumigatus*, *Rhizopus stolonifer*, *Fusarium solani*, and *Candida albicans* in vitro and confimed sy an applied practical study on lung (pulmonary) tissues of infected rats after their treatment with pathogenic *Aspergillus flavus* and also treatment with Musk and sidr leaves as natural sources.

2. Materials and Methods:

2.1.Materials:

2.1.1- Musk:

Musk is formed of many compounds, the main compound which causes the odour is muskone, and contain 1.4% volatile oil with black to brown color, estroil hormones, the most important were musk pyridine in addition to some alkaloids and enzymes, and is used as powder. The natural black animal musk extracted from the umbilicus of deer. Musk was obtained from Korashi Stores KSA- Jeddah and was preserved in natural environmental circumstances at temperature 25 – 28 C°.

2.1.2.Sidr(Zizyphus spina- Christi):

Rhamnaceae- Rhamnales.

They are huge long living trees with alternate leaves with hermaphrodite flower. The flower is mono ecious having sweet taste and fruits are drupe were type. The plant is used as blood filter and in treatment of diarrhea and gall bladder. Leaves and cortex are used in treatment of wounds and skin diseases. Sidr leaves were collected from trees in Jeddah.

2.1.3-Female rats:

Albino mice (Mus musculus) strain MFI were used Their weight varied between 150 – 170 gm. They were obtained from king Fahd research medical center - King Abd El Aziz University- Jeddah. They were injected intra peritonealy peritoneal with the pathogenic fungus *A. flavus*.

2.1.4-The Experimental fungi:

They belonged to the opportunistic fungi *Aspergillus flavus*, *Aspergillus fumigatus*, *Rhizopus stolonifer*, *Fusarium solani* and *Candida albicans*. They were obtained from Mircen center of college of Agriculture Ain Shams University. Egypt. They were incubated at 25 2 C°.

2.1.5-Media:

Sabouraud Dextrose Agar(S.D.A) media: 65 gm of the media were used. The media was previously prepared oxid CM41/ liter distilled water, then sterilized in wet sterilization by autoclave at 15 liter/ square inch for 20 minutes.

2.2.Methods:

2.2.1-preparation of (therapeutic) material:

a- Musk:

Hydrous extracts was prepared of black musk from deer musk with concentration of 0.02% given to rats with dose of 1 ml/ kg body weight.

b-Sidr leaves:

Sidr plants were washed and left to dry, then after washing and grinding 100 gm/200ml were taken for distilled and sterilized water (Adzu *et al*., 2001) and after 24 hours filtered and preserved in dark glasses in refrigerator till used. That was given to rats in dose of 1 ml/kg body weight.

2.2.2- Microbiological examination:

a)Preparation of suspensions of pathogenic fungi and yeast:

The experimental fungal spore's suspension was prepared from deviated growth aged 10 days of pathogenic fungi and yeast on solid Sabouraud Dextrose media, that was done by adding 5 ml of sterile distilled water on the deviated growth by using a sterile needle, then fungus was stirred and the spore suspension of the deviated growth was collected in glass flask.

b) Effect of musk powder and sidr leaves on the experimental fungal radial growth:

The experiment was done to know the extent musk and sidr leaves contain effective drugs that can suppress of pathogenic fungi.

Three techniques were done:

***The first**, 2.0 gm of sidr leaves were dried, grind then put in sterile sac, distilled water was added to make paste.

***The second** technique was by adding a distilled amount of sterile water to 1 gm musk powder.

***The third** technique was the same but with addition of 2.0 gm sidr leaves and 1.0 gm musk powder together, distilled water was added to form paste. All formed pastes were inserted sporadically each one alone in the middle of Petri dishes. On the other hand, solid Sabouraud media was added in Petri dish and by using cork borer fertilized by a disk of the experimental fungus aged 5 days and with diameter 6.0 m and was inserted in the middle. The part of the dish containing the media and fertilized was put upside down on the similar part containing the paste of sidr leaves and musk extract. The two parts were sticked together by sticking tap then the dishes were incubated for 6 days at temperature 25 2 C° (Bardin *et al*, 2004).

c) Effect of hydrous musk and sidr leaves on the experimental opportunistic fungal growth:

Agar-well diffusion method was used according to (Collins., 1989) to study the effect of hydrous musk extract of the experimental material on fungal growth suppression. One ml of spore suspension of each fungus was added to 50 ml solid Sabouraud media before freezing with good shaking then Sabouraud media were distributed in Petri dish and the dishes were left to solidify. The dishes were removed by sterile invasive metallic with diameter of 6 ml in the middle of each Petri dish. In each pore in the Petri dish 0.5 ml hydrous extract of musk and sidr with 25% concentration and their mixture after the extracts were sterilized by bacterial filter then were incubated in Petri dish at temperature of 25 C°, then growth diameter was measured daily for 6 days for 6 consecutive times for each fungus, and was compared with control samples.

2.2. 3-Study on experimental animals

a-Histological study by light Microscopes (Bancroft and Gamble, 2002)

Lungs were dissected from rats and fixed by following standard methods of dehydration and clearing.Then the samples were embedded in paraffin and cut with 3 micron thickness of the control samples and samples treated and infected. Lung tissues were fixed by neutral buffered neutral formalin. Sections were stained with haematoxylin and eosin stain.

b-Fixatives used for study:

Neutral buffered solutions for histological study by light Microscope.

c-Staining used for the study:

Haematoxylin and Eosin stain (H&E) The stain gives clear cytoplasm differentiation and nuclear and gives good idea about histological structure of the samples of the study and reveals some pathogenic changes.

2.2.4-Statistical study:

Effect of different techniques by using Spsspc ++ program to find T- Test.(Abo- Zied., 2003)

3.Results:

3.1- Microbiological study:

a) Effect of musk and sidr on radial growth rate of the experimental fungi:

Table 1 shows decreased percentage of Diameter growth of experimental fungi in all treated groups at the end of incubation period. It was also noted that musk treatment gave the highest percentage growth suppression as it reached 74.61% and 68.76% and 71.75% for all fungi *Aspergillus flavus*, *Aspergillus fumigatus*, and *Fusarium solani* respectively while it reached 67.80% and 56.92% for *Rhizopus stolonifer* and *Candida albicans* compared to control samples(Fig. 1).

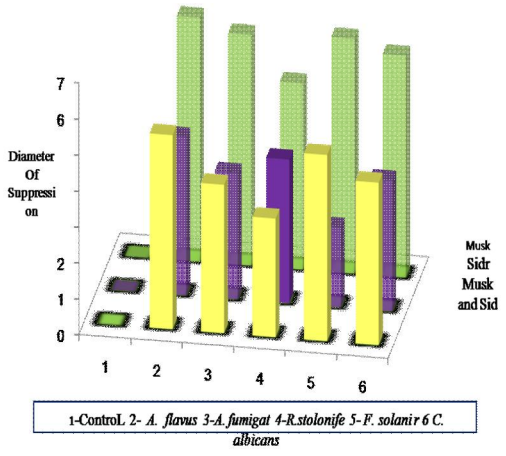

Fig.(1) Effect of musk and sidr leaves extracts on the radial growth of the experimental opportunistic fungi at concentration 25% after 6 days (mm/disc, means ± SE).

Table (1). Effect of musk and sidr leaves extracts on the radial growth of the experimental opportunistic fungi at concentration 25% after 6 days (mm/disc, means ± SE)

Treatment	MUSK		Sidr		Musk and Sidr	
	Diameter of Suppression	Percentage of Suppression (%)	Diameter of Suppression	Percentage of Suppression (%)	Diameter of Suppression	Percentage of Suppression (%)
Control	0.0	0.0	0.0	0.0	0.0	0.0
Aspergillus flavus	6.79±0.42**	74.61	4.40±0.23	48.35	5.40±0.50**	59.34
Aspergillus fumigate	6.42±0.00**	68.76	3.51±0.10**	38.57	4.13±0.40*	45.38
Rhizopus stolonifer	5.18±0.12*	56.92	4.00±0.13	43.95	3.30±0.02**	36.81
Fusarium solani	6.53±1.05**	71.57	2.22±0.21**	24.39	5.18±0.30	56.92
Candida albicans	6.17±0.30	67.80	3.64±0.08*	40.00	4.25±0.01*	49.67

*significant at 5%; **significant at 1%

b) Effect of musk and sidr leaves extract on the experimental fungi:

The previous experiment was confirmed by another study but with using hydrous extracts of musk and sidr leaves, suppression of fungal growth around the pore forming inhibition zone empty of fungal growth and with different diameter differ with the different fungal species and the resistant strength of the extract.

The largest area empty of fungal growth was seen with *Aspergillus flavus* and *Fusarium solani*, followed by *Aspergillus fumigatus* and *Candida albicans* then finally with *Rhizopus stolonifer* respectively when comparing with controlled group which had no extract and fungal growth had appeared completely around the pore (Fig. 2-5). The results can be a positive indicator to use musk and sidr in treatment of fungal diseases caused by the fungi studied in this research.

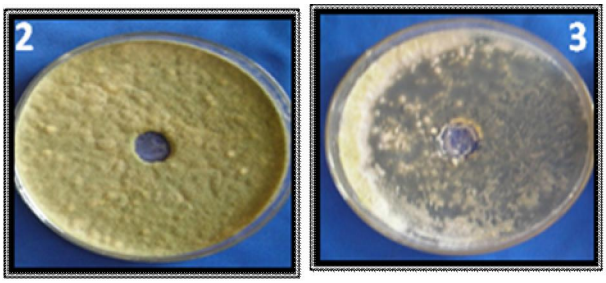

Fig.(2) Shows the control sample of the pathogenic fungus *Aspergillus flavus* with a plate full of growing fungus and inhibition zone of the *A. flavus* around the well containing musk(3).

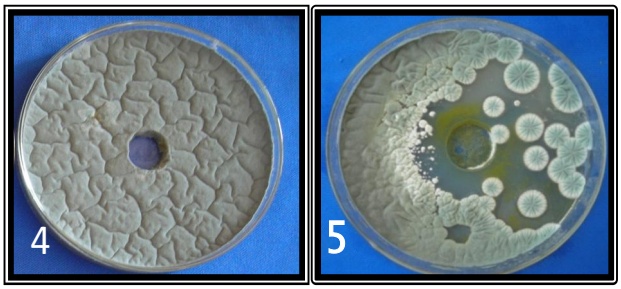

Fig.(3) Shows the control sample of the pathogenic fungus *Aspergillus fumigatus* where the plate is full of growing fungus and inhibition zone of *A. fumigatus* around the well containing musk(5).

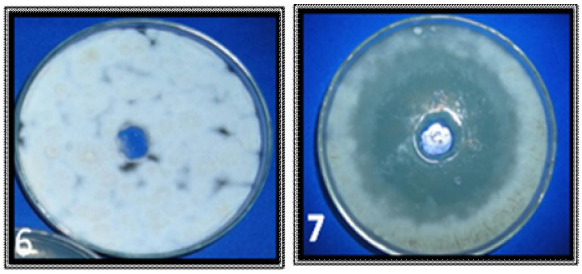

Fig.(4) Shows control sample of *Fusarium solani* where the plate is full of growing fungus and inhibition zone of *Fusarium solani* around the pore containing musk(7).

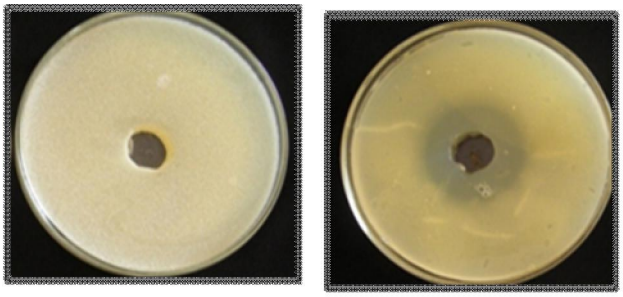

Fig.(5) Control sample of *Candida albicans* showing full plate of growing yeast and inhibition zone of *C. albicans* around the well containing musk (9).

3.2- Histological examination of rat lung:

Lung is formed of alveoli, alveolar sacs, bronchi and bronchioles besides blood vessels, nerve fibers and few connective tissues. Histological examination (Fig. 6) showed the normal control rat lung structure. The lung was formed of bronchioles, terminal bronchioles, respiratory bronchioles and alveolar ducts and alveolar sacs.

a) Control group:

Histological examination of bronchi of control rat lung showed that it is lined by endothelial tall columnar ciliated epithelial cells with few goblet cells. The basal layer was surrounded by smooth muscle layer, the bronchioles have no cartilage and join elastic radiating fibers to surround lung tissue (Fig. 7). Histological examination of the terminal bronchioles (Fig. 8) showed that it was lined by cuboid or simple columnar cells with no goblet cells and having clara cells instead. Clara cells are columnar cells with secretary apical granules, then muscle layer surrounded the smooth plate which surround. Histological examination of bronchioles showed that they were lined by non ciliated cubical cells with few clara cells. No goblet cells are seen, a layer of smooth muscles surrounding a connective elastic tissue layer surrounded. Each respiratory bronchiole is divided into many alveolar ducts that end with alveolar sacs and opened respectively in many alveoli (Fig.9). Each alveolus has opened in one side, alveolar wall had three histological components of surface epithelial cells and tissue blood vessels. Epithelial tissue lined all alveoli and is formed of two types of cells. Squamons cells type I alveolar cells (type I pneumocytes) which predominated the surface lining, and Alveolar cells type II (type II pneumocytes) which occupied small area of the alveolar surface.

Blood vessels surrounding the alveolar walls and branched to form a close arrangement similar to basket around each sac. Endothelial cells of the alveolar sacs are found on the convex side of basal membrane while cells ling the capillary vessels lie on the concave side near to the red blood cells inside the capillary vessels (Fig. 10).

b) Control group infected with experimental fungus:

Histological examination of the infected sample with the experimental fungus showed that the cells shape was disturbed in lung tissue. The histopathological changes were seen all over the lung component, bronchi, bronchioles, sacs were all affected (Fig. 11).

Large areas of fibrous tissue were seen and spread all over the field (Fig. 12). Changes were in the form of dilated and joined some of the terminal bronchioles (Fig. 13). Areas of tissue lysis, congestion, hemolysis (Fig. 14) and in other area of pulmonary tissue, there were some damaged terminal bronchioles with lost normal architecture (Fig. 15). Those pathogenic changes lead to morphological and physiological changes due to fungal toxicity.

c) Musk and sidr treated group:

Histological examination of lung tissue in rats treated with musk and sidr treated each one alone or treated with both musk and sidr showed no harmful negative effects on lung tissues. Sections were similar to control group. Histological examination of the section (Figs. 16 and 17) showed lungs of rats treated with musk only, (Figs.18 and 19) showed lungs of rats treated with sidr only, and (Figs.20 and 21) showed rats treated with musk and sidr together.

d) The fungal infected group treated with musk and sidr:

Treatment with musk alone of the infected rats with the experimental fungus, or treatment with sidr alone or those which were treated_with both musk and sidr gave positive effects in lung tissue regeneration similar to normal structure. Improvement was clear in most of the tissue components in structure such as bronchi, bronchioles, alveoli (Figs. 22– 25) treated with musk alone. Also (Figs.26– 27) sidr only treated showed that the lungs were similar as. Histological examination of rat lungs after musk and sidr treated together are showed (Figs. 28 – 33).The results showed the possibility to use musk and sidr as a curative and treatment from the experimental fungus causing lung toxicity. This research showed for the first time a practical scientific application for uses of musk and sidr as a treatment to cure, manage and prevent fungal puemtoxicocis which is one stage of cancer lung.

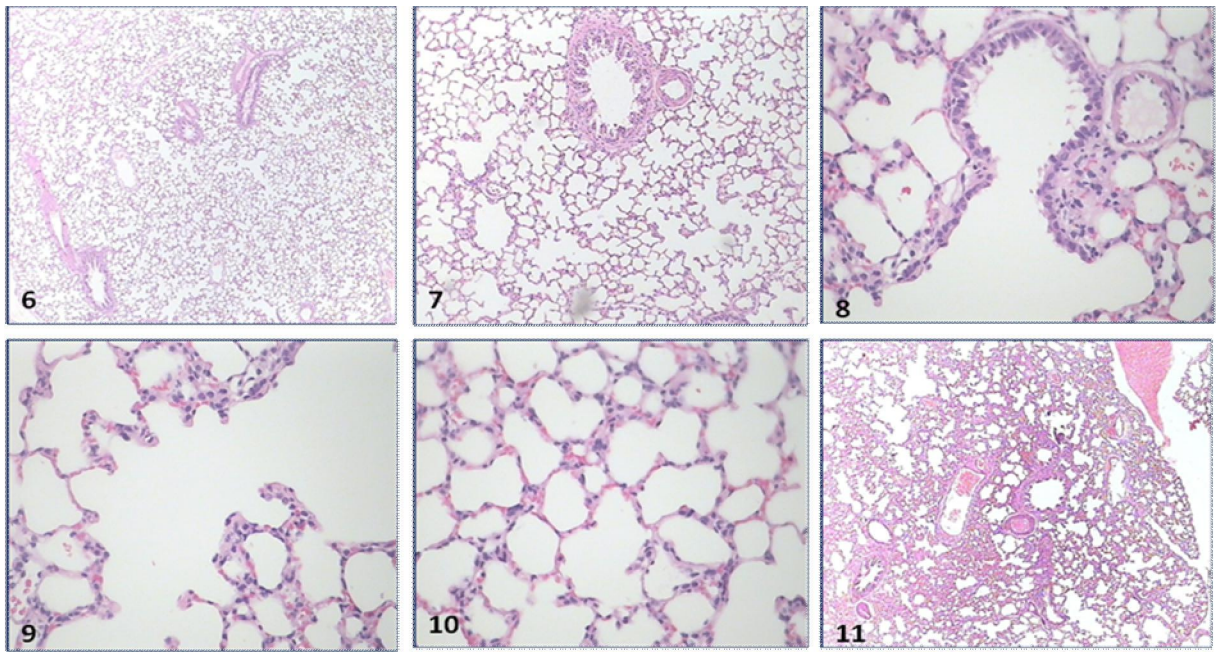

Fig. (6) Section of control lung showing general view of lung tissue. H & E(X40)
Fig. (7) Section of control lung showing bronchioles and blood vessels. H & E(X100)
Fig. (8) Section of control lung showing terminal bronchioles and bronchi. H & E(X400)
Fig. (9) Section of control lung showing alveolar canal and alveoli H & E(X400)
Fig.(10) Section in control lung showing alveolar sacs and alveoli. H & E(X400)
Fig. (11) Section in infected lung by the experimental pathogenic fungus showing the general view of the lung tissue. H & E(X40)

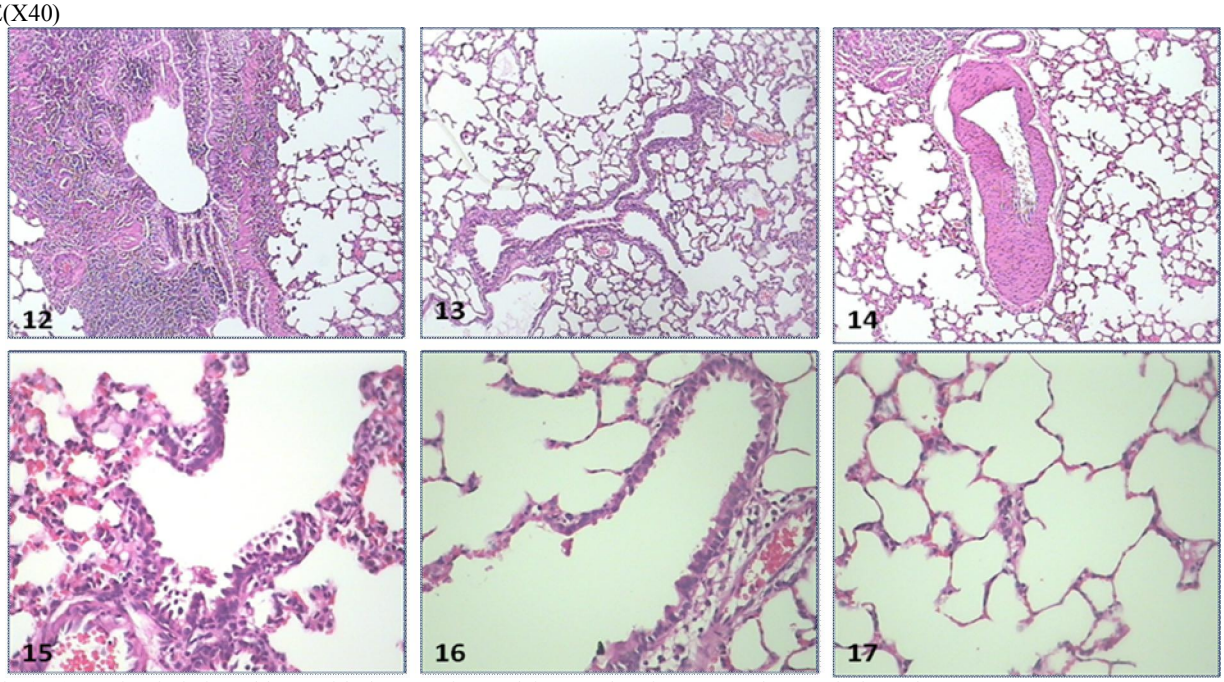

Fig.(12) Section in infected lung with the experimental fungus showing severe damage in lung tissue. H & E(X100)
Fig. (13) Section of infected lung tissue with pathogenic fungus showing damage and joined terminal bronchioles and bronchi. H & E(X100)
Fig.(14) Section of infected lung by the experimental fungus showing damage of blood vessel with dilatation and congestion H & E(X100)
Fig. (15) Section in the infected lung by the experimental fungus showing damage of the terminal bronchi. H & E(X400)
Fig. (16) Section of lung treated with musk only showing the terminal bronchi and alveolar canal. H & E(X400)
Fig. (17) Showing section in lung treated with musk only showing alveolar sacs and alveoli. H & E(X400)

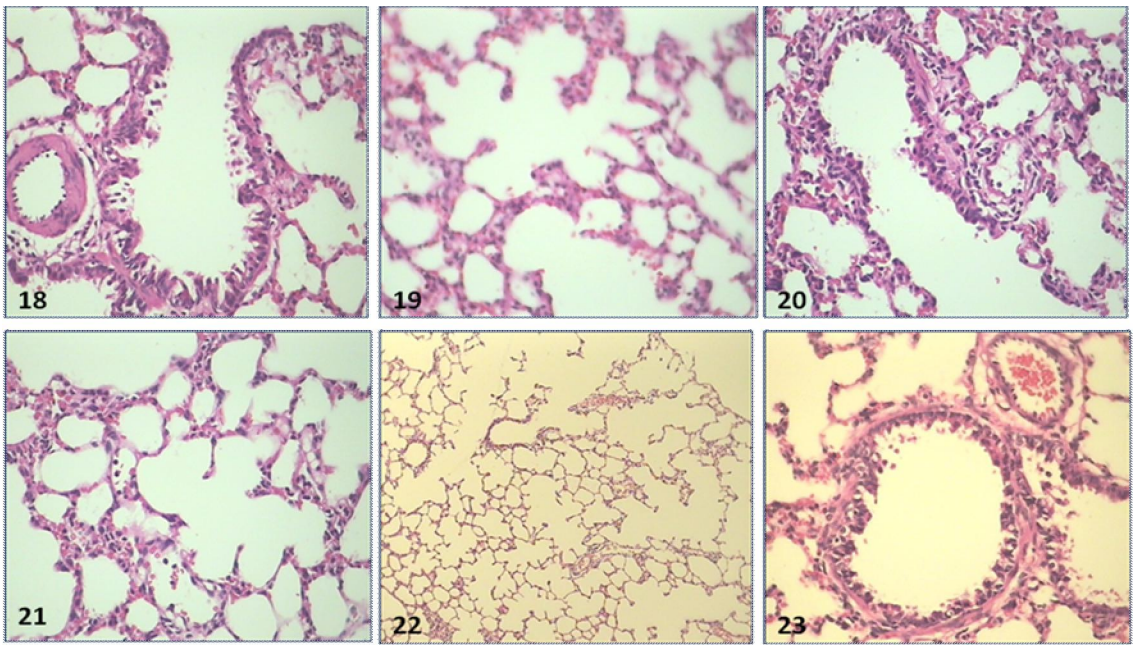

Fig. (18) Section of lung treated with sidr only showing terminal bronchioles and blood vessels. H & E(X400)
Fig. (19) Section of lung treated with sidr only showing the alveolar sacs and alveoli. H & E(X400)
Fig. (20) Section of lung treated with musk and sidr showing terminal bronchioles. H & E(X400)
Fig. (21) Section in lung treated with musk and sidr showing alveolar sacs and alveoli. H & E(X400)
Fig.(22) Section of infected lung with the experimental fungus and treated with musk only showing general view of the lung tissue. H & E(X100)
Fig. (23) Section of infected lung with the experimental fungus and treated with musk only showing bronchioles and blood vessels. H & E(X400)

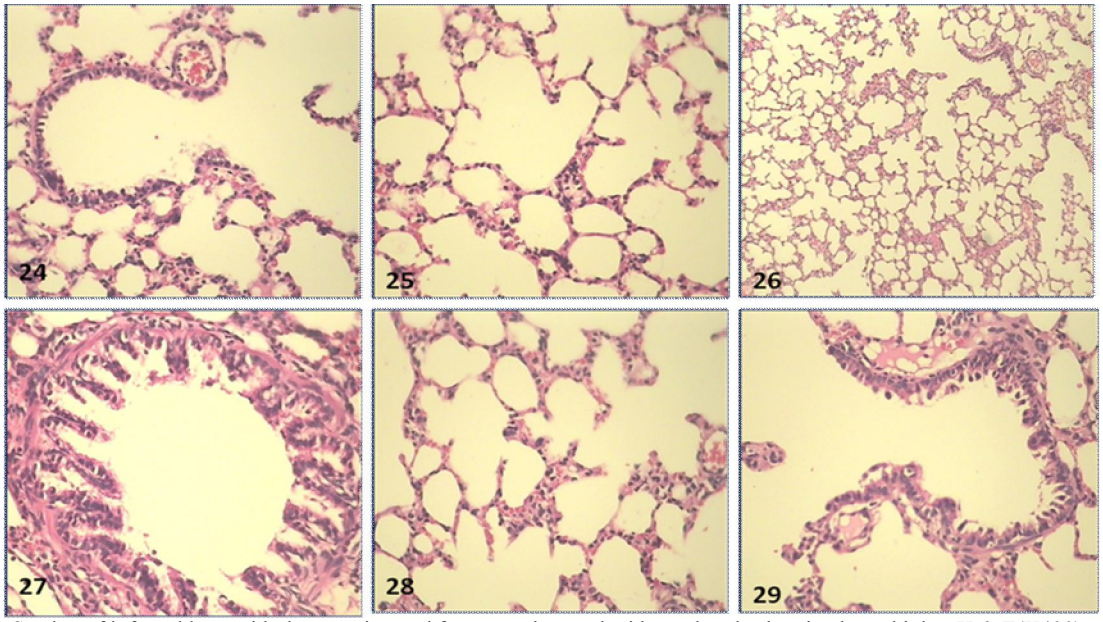

Fig. (24) Section of infected lung with the experimental fungus and treated with musk only showing bronchioles. H & E(X400)
Fig. (25) Section of lung infected with experimental fungus and treated with musk only showing alveolar sacs and alveoli. H & E(X400)
Fig. (26) Section of lung infected with pathogenic experimental fungus treated with sidr only showing general view of the lung tissue. H & E(X100)
Fig. (27) Section of lung infected with pathogenic experimental fungus and treated with sidr only showing bronchioles. H & E(X400)
Fig. (28) Section of lung infected with the experimental fungus and treated with sidr only showing terminal bronchioles. H & E(X400)
Fig. (29) Section of lung infected with experimental fungus and treated with sidr only showing alveolar sacs and alveoli. H & E(X400)

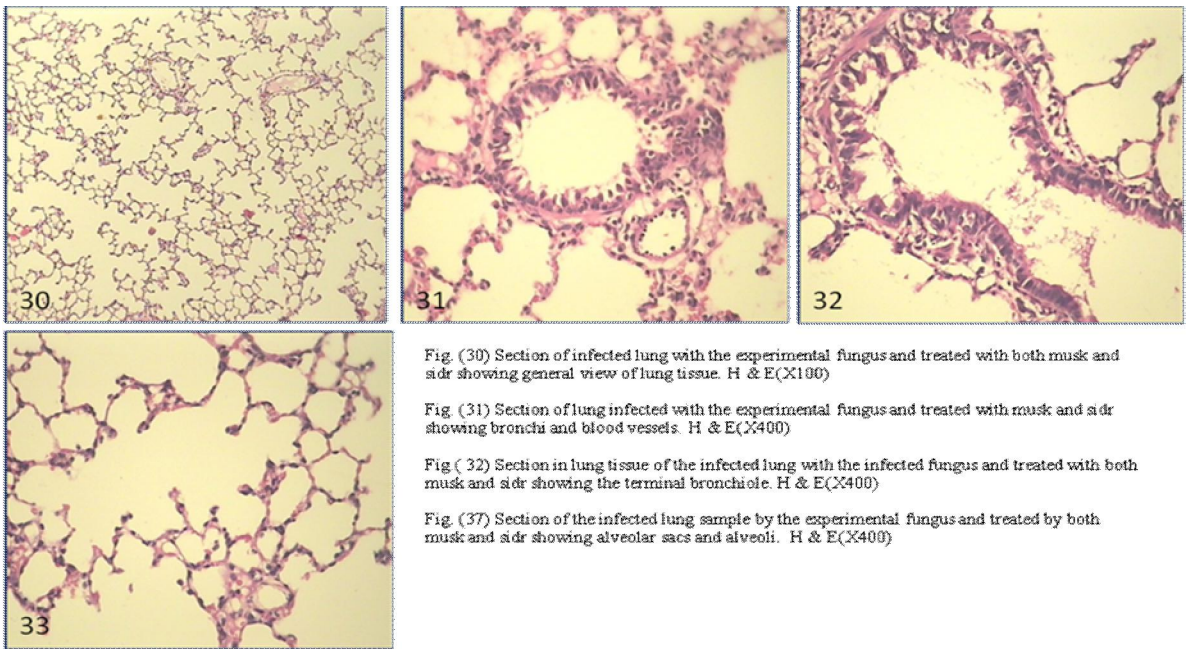

Fig. (30) Section of infected lung with the experimental fungus and treated with both musk and sidr showing general view of lung tissue. H & E(X100)

Fig. (31) Section of lung infected with the experimental fungus and treated with musk and sidr showing bronchi and blood vessels. H & E(X400)

Fig (32) Section in lung tissue of the infected lung with the infected fungus and treated with both musk and sidr showing the terminal bronchiole. H & E(X400)

Fig. (37) Section of the infected lung sample by the experimental fungus and treated by both musk and sidr showing alveolar sacs and alveoli. H & E(X400)

4.Discussion:

Aspergillus is a widely spread fungus found in the natural environment. Spores are found in soil and air. They grow in any non living media most species are harmful and pathogenic to animal and human and the diseases caused by *Aspergillus* collectively are referred to as Aspergillosis. (Al Rahma., 1993). One of those fungi is *A. fumigatus* that was one of the opportunistic fungi that caused severe life threatening infection in cases of patients suffering from immune deficiency. The source of the respiratory infection are the fungal spores preset in air and enter the lung which is the first line of defense which can localize and kill the spores after cellular infiltration as the lung can be an important defense line against *Aspergillus* (Luther *et al*., 2007). Table (1) shows suppression extent due to sidr leaves effect on the radial growth of the experimental fungal. That agreed with (Adzu *et al*., 2001) and (Shahat *et al*., 2001) that sidr can be used as a disinfectant of wound and treatment of boils and curubuncle and can be used in insomnia and as antifungul, anti bacterial and anti viral (Han *et al*., 2005; Suksamrarn *et al*., 2006). Efficiency of the plant is referred to its content of many efficient subjects as flavonoids, peptids and peptide alkaloids and saponin and sugars (lactose, glucose galactose) as well as glycosides and vitamins A and C (El Din *et al*., 1996; Adzu *et al*., 2001; Abdel-Zaher *et al*., 2005). In addition to fermentation process by microbes accompanying them. That lead to break and spread out of large amount of sulphur that leads to toxicity of pathogenic organism and their spores, or may be due to fungal antagonistic action due to bio resistance of the accompanying microbes that had been used in getting rid of many harmful microbes (Abo-Arkoub, 2002) or may be due to suppression due to some Aliopalthetic that interfere directly with the pathogenic fungal growth that lead to their suppression such subjects are phenols Aliopalthetic. That is in agreement with the role of the plant rubbish and of some other plants (Pavlou and Vacalounahis, 2005).

Sheik., (2008) pointed out that some plant extract had great role in suppression of *Fusarium solani* suppression that causes rotten seeds and roots. Musk had great role in suppression of the opportunistic fungal growth. Musk action can be caused by chemical structure of musk as it contained high volatile oils percentage and contain sterol hormones in which the most important was muskopyridine besides some alkaloids and enzymes that can elongate lag phase or affect mitotic divisions and elongate fungal cells. Musk can also decrease growth due to suppression of spores or due to formation of complex toxic substance formed after joining the protein with musk inside the cells and enzyme activity suppression can affect negatively the metabolic processes of the pathogenic fungus during the growth period.

That is similar to the role of fungicidal substances that cause suppression (Youssuf *et al*., 2003; Karadimos *et al*.,2005). Table (1) shows affection of experimental fungi by musk.The fungus was *Rhizopus stolonifer* show more resistance compared with control sample. Resistance can be due to decreased permeability of musk component through cell wall and endoplasmic membrane for that fungus especially more than in other fungi which are

highly sensitive to its presence between their growth as the percentage for cell wall protein, mannose, cellulose, kitine, glucan differed according to species of fungus (Brady *et al*., 1994), and it is possible that the pathogenic fungus had a rapid growth rate that can help in re growth more rapidly than other fungi (Abd –ElHameed., 2000).

Jaeffar and Jaeffar, (1994) mentioned that Aspergillus lung diseases are present with different. Bennett., (1979) mentioned that *A. flavus* grow in human tissues or through body respiratory spores and that is what is called Aspergillosis Bennett.,(1980) mentioned the role played by Aspergillus in non spread lung diseases. Hyphea can cause bronchoconstriction due to the fungal toxins. Aspergillosis was specially found only in immuno suppressed patients studies made by Chih-Chinglai *et al.,* (2007) invasive Pulmonary Aspergillosis was diagnosed in 26 probable or settele in patients. Hematological signs were present. Most fungal infection was *Aspergillus fumigates* 46% followed by *Aspergillus flavus* 23%. Morality rate was 62% and mono contrast and multi contrast retrograde analysis showed that blood coagulation spread in blood vessels was the only factor that caused death due to Pulmonary Aspergillosis. IPA, the toxic subject Gliotoxin was measured in experimental Aspergillosis and human in both lungs. The rate was 1.662 ± 3.976 Aspergillosis gram of gram of tissue and blood.The rate was found 30.28 ± 36.5 Nano gram/m, in case of rat suffering from spreading Pulmonary Aspergillosis (Lewis *et al.,* 2005). Lai *et al.,* (2007) mentioned that blood coagulation spread in blood vessels was the only factor that causes death due to Pulmonary Aspergillosis. Bronchi and lungs could be affected by toxins that affected pleura membrane. Air could enter to pleura and cause collapse of Pulmonary sacs (Al Gammas, 1983).

Hawgood., (1997) and Gunther *et al.,* (1999) pointed out that the importance of pulmonary surfactant exchange came from its role in keeping and preventing distended alveoli collapse by decreasing the alveolar surface tension,Harrison., (2004) and Davidson., (2006) Points out that lung diseases caused by fungal infection were accompanied by lung pains, pain in the shoulder, and respiratory difficulties and a dry cough at the beginning of the disease and accompanied by symptoms of fever, loss of appetite, which were the diagnostic signs of obstructive lung diseases Pneumonia and vesicular constriction associated with pulmonary odema and cellular infiltration of air sacs, besides increase in the number of blood cells in the lung.

The importance to use musk and sidr in reducing pathogenic fungal growth rate and the impact on metabolic and enzymatic activity and therefore reduction of the disease was shown clearly. That will encourage further researches of the natural materials to antagonize fungal pathogens and replace unnatural synthetic and chemical drugs.

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