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A new drug formula for pneumonia and severe seasonal flu; a promising drug for eradicate COVID19

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ABSTRACT

World Health Organization (WHO) well-known pleiotropic antiviral compounds. This study was designed to evaluate the effects of herbal drug combination in treatment of pneumonia, severe respiratory distress, and severe flu and recently for COVID19. The treatment phase includes 12 days period of herbal drug mixture (X). Results showed the activity of herbal drug in eradication of COVID19, pneumonia and severe seasonalful.

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1. Introduction

The Dietary Supplement Health and Education Act (DSHEA) of 1994 classifies herbs as dietary supplements (Dietary [4,11–15]. Dietary supplements can be produced, sold, and marketed without first demonstrating safety and efficacy, as is required for pharmaceutical drugs (Dietary [4]. Because herbs are plants, they are often perceived as “natural” and therefore safe ([5,9,10]. Table 1. Table 2. Table 3. Table 4. Fig. 1.

2. The herbal formula

The novel formula was created by combining 7 herbs (*Tetraclinis articulata*, *eucalyptus*, *thymus vulgaris*, *syzygium aromaticum*, *illicium verum*, *boswellia carterii*, *mentha*) that have commonly been used in the prevention and treatment of different diseases. >14 ingredients noted in the modern herbal pharmacopoeia to have strong antiviral properties were in the components of drug. The entire drug formula therefore consisted of 7 herbs. (Alhayani, B. 2017)

3. Subjects and data collection methods

Volunteer's patients who were diagnosed by respiratory disease specialist were recruited for the study. the study patients received

2 bottles of the herbal preparation free of charge for each one and were learn the methods of administration, the herbal drug mixture every day for 12 days.

4. Exclusion criteria included

Note: previously we used this drug formula in the treatment of pneumonia, severe respiratory distress, severe seasonal flu, and after the occurrence of COVID19 pandemic, we developed the formula to treat the COVID19. (Alhayani, B. 2014)

4.1. Detection of the drug components

Drug materials were obtained from traditional medicine suppliers in Iraq.

4.2. Pre-clinical experiment: Safety of drug preparation

4.2.1. Median lethal dose (LD50)

Thirty adult female albino BALB/C mice (6–8 weeks, range of body weight = 20–25 g, 4 mice in each group) were used to determine the S/C median lethal dose (LD₅₀) of drug (aqueous extracts). The animals were kept in well air-condition rooms at the private animal house, given pellets of balanced specially prepared animal feed and water. Graded doses of drug extracts in 0.1 ml PBS were administered orally to each one animal daily, a series of concentrations of local herb extract employed by ([32].). (Alhayani, B.2020)

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Table 1
Composition of aqueous-ethanolic extract herbal drug mixture.

No.	Name of compound	Molecular formula	Peak area %
1	O-cymene	C10H14	1.16
2	D-limonene	C10H16	0.25
3	p-cineol	C10H18O	2.47
4	Neodihydrocareveol	C12H20O2	1.43
5	Gamma- terpinen	C10H16	0.58
6	Caprylic acid	C8H18O	2.27
7	linalool	C10H18O	1.2
8	gingerol	C17H26O4	7.5
9	Isopinocarveol	C10H16O	0.53
10	Shikimic	C7H10O5	2.57
11	Carvomenthenol	C10H18O	1.29
12	Alfa-thujone	C10H16O	3.16
13	Alfa-Terpineol	C10H18O	0.84
14	Allylguaiacol	C10H12O2	21.78
15	Allicin	C6H10S2O	3.65
16	p-cumic aldehyde	C10H12O	0.65
17	p-anisaldehyde	C10H16	1.12
18	Anisol,p-propenyl-	C10H12O	5.1
19	Estragol	C10H12O	2.2
20	Carvacrol	C10H14	8.3
21	Curcumin	C21H20O6	2.12
22	Gamma-elemene	C10H18O	0.91
23	Linalyl butyrate	C14H24O2	10.2
24	Trifolitin	C15H10O6	2.7
25	Beta-pinene	C10H16	9.2
26	Myrcitein	C15H10O8	4.9
27	α-bisabolene	C15H24	2.78
28	B-caryophellene	C15H24	2.0
29	Farnesol	C15H26O	2.05
30	B-eudesmol	C15H26O	2.6
31	Vinilylacetone	C11H14O3	2.1

4.3. Clinical trial

4.3.1. Test Product, dose and mode of administration

Drug materials were obtained from traditional medicine suppliers in Iraq, 3.5gm of herbal drug mixture was boiled in 150 ml water, taken 4 times daily and other part taken as inhalation by nebulizer 4–7 time daily depending on severity of disease.

4.3.2. Methodology

1. **Ten** patients with **COVID19**, age ranged (25–70 years); 12 days for each course treatment, a randomized study to examine efficacy of herbal drug in patients with **COVID19**.
2. Twenty five patients with pneumonia suffering from severe respiratory distress, age ranged (15–45 years); 12 days for each course treatment, a randomized study to examine efficacy of drug preparation.
3. Thirty one patients with severe seasonal flu, age ranged (15–47 years); 12 days for each course treatment, a randomized study to examine efficacy of herbal drug .

The whole time of study was 8 month from (February 2019-march 2020).(Alhayani, B.2020)

Table 2
LD50 of herbal drug mixture (aqueous extract) in normal mice.

Extract	Dose mg/kg	Results of test 1 2 3 4	Series of results	K-value	D- value	LD50mg/kg
Aqueous	3500	0				0000
	4000		0			1.000
	4500			0		500
	5000				0	5500

5. Results and discussion

The aqueous-ethanolic extract, and 50 gms of the herb gave 15 gms of dark yellow extract 30% yield.

5.1. Identification of herbal drug constituents

The aqueous-ethanolic extract
Thirty one compounds were identified by GC/MS .

5.2. Pri-clinical study

Although the components of the herbal drug are within the permissible FDA regulations and provide global studies related the safety of the components of the herbal drug, however we have studied the toxicity of the drug on laboratory animals.

Median Lethal Dose (LD50):

$$LD50 = Xf + Kd$$

Xf = Latest dose used, k = table value

d = amount of increase and decrease in a given dose

$$LD50 = 5000 + (1.000 \times 500)$$

$$LD50 (\text{Aqueous extract}) = 5500 \text{ mg/kg body Wt.}$$

5.3. Clinical trial

The data in the table (3) revealed that the most of patient were recovered, and there was a highly significant difference among the recovered patient in comparison with pre-treatment patients at $P < 0.03$) in both treated group (pneumonia & severe flu) respectively.

The results in table (4) showed that all the treated patients were completely recovered in spite of non-significant difference between pre-treated and recovered patients.

6. Discussion

Already the interested novel herbal drug has been used by a group of patients suffering from pneumonia with severe respiratory distress, as well as patients with severe seasonal flu. The

data in tables (3) reveals that there were a highly incidence of healing as a results of herbal drug treatment with no side effect, and most of the patients were completely returns to their good health within 3–9 days, the improvement in the clinical situation began with the first doses of treatment .

The good news is that this novel herbal drug has been tested in volunteer’s patients with COVID19. The preliminary results showed its effective effect in eradicating the COVID19 in short period.

The characteristic composition of this herbal drug makes it effective in treating respiratory disease, especially COVID19.

The GC/MS data cleared that the interested herbal drug contains a cocktail of compounds that works in different mechanism. The effectiveness of the interested novel herbal drug in eradicating the respiratory viruses especially **novel corona virus** is due to contains many well-known pleiotropic antiviral compounds.

Table 3
Patients treated with herbal drug mixture .

Disease	Age range	No. of patient	Recovered patients	C.S
pneumonia	15–25	8	8	P = 0.01
	26–36	13	11	
	<45	4	3	
Severe flu	15–25	12	11	
	26–36	8	6	
	37–47	11	9	

Table 4
COVID19 patients treated with herbal drug mixture .

Age (years)	No. of patient	%	Healing events	%	C.S
25–35	3	30	3	30	P = 0.182
36–46	2	20	2	20	
47–57	4	40	4	40	
70>	1	10	1	10	
total	10	100	10	100	

P < 0.03 (highly significant); P > 0.05 (Non-significant)

The virus particle have 2 surface antigen, The enzyme neuraminidase (NA) is an attractive target for antiviral strategy due to its essential role in the pathogenicity of many respiratory viruses (Serkedjieva et al., 2007).

The kampferol a compound of the herbal drug is the most famous antiviral compound which neutralize and reduce the infectivity of influenza viruses A and B ([8] . Also the drug contains a Myricetin which considered a SARS–CoV helicase inhibitor (Yu, et al., 2012) . The gingerol and zingerone were inhibited of virus cell infusion and prevent viral replication of H1N1 and also could

stimulate mucosal cells to secrete IFN-β that possibly contributed to counteracting viral infection of human respiratory syncytial virus in human respiratory tract cell lines [3] B ([19]. The β-pinene has high macrophage immunomodulatory efficacies and therefore contributes in killing bronchitis viruses (Lumaret et al., 2001).

By the other hand the presence of α-terpineol and thujone which induce leukocyte and cytokine, increases antibody response against virus ([2]. A phenylpropanoids and sesquiterpenes like γ-bisabolene, β-caryophellene, farnesol and β-eudesmol that present in herbal drug directly inactivate herpes virus and might interfere with virion envelope structures or mask viral structures that are necessary for adsorption or entry into host cells ([29]. Also the curcumin compound in the herbal drug formula inhibits severe acute respiratory syndrome coronavirus ([33] and rhinovirus ([27]. The allylguaiacol compound present in the drug formula showed significant inhibitory activity against HCV protease ([7].

The shikimic acid present in the drug formula which is considered a starting material for the synthesis of Tamiflu will inhibit neuraminidase and contribute in eradication of swine flu virus H1N1 ([26] & McKimm 2013) .

The anti-inflammatory effects of interested drug is due to presence so many compounds; Carvacrol present in herbal drug may inhibit production of prostaglandin E₂

Furthermore , the presence of many compounds in the drug formula like curcumin ,α-limonene ([1].

The bronchodilatory effect of herbal drug is due to contains many compound which led to relaxation of smooth muscles in bronchi ([20] and Oluwagbemiga et al.,2017).

The novel herbal drug also contains many compounds work as sedative, anxiolytic and relieve panic condition that may affect the patients with COVID19 (Ka Young et al., 2014; Diogo et al.,2019 ; [6] .

Finally the herbal drug contains many compound acts as antibacterial that may eradicate the opportunistic bacteria that infect COVID19 patients ([45] ; Sedarnawati et al.,2009)

7. Conclusion

The novel combination of the drug materials gives amazing effects. Also the presence variety of antiviral compounds that acts with different mechanisms can able to eradicate the highly mutated viruses like **novel corona virus-19**. The bronchodilator,

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Fig. 1.

anti-inflammatory, anti-bacterial, anxiolytic, sedative and potent antioxidant effects of herbal drug is due to contain variety of active compounds.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Further Reading

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