Available online on 15.05.2019 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Open Access Research Article

Safety Study of a Non-pharmacopial Compound Unani Formulation

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ABSTRACT

Herbal drugs are in use since antiquity with an assumption that they are almost devoid of side effects. But many reports published in recent years suggest that they are liable to produce a number of side effects. Keeping it in view WHO has proposed a guideline of safety study herbal drugs and food products. It includes the determination of Aflatoxin, heavy metals, pesticide residue and Microbial load. A non pharmacopoeal Unani formulation containing Tukhm-e-konch, (*Mucuna pruriens),* Khulanjan, *(Alpinia galangal),* Salabmishri, *(Orchis latifolia),* is commonly used for sex improving effect. This combination has also been proved effective in experimental studies but the safety study as per WHO guidelines has not been conducted. Therefore the present study was carried out to determine the presence or absence of the toxic components in the test drug.The protocol suggested by WHO was used during the study. The combination was found to be safe as all the component was found within the permissible limits.

Keywords: Safety study, NPCF, Aflatoxin.

Article Info: Received 26 March 2019; Review Completed 09 May 2019; Accepted 12 May 2019; Available online 15 May 2019

Cite this article as:

Ali M, Khan NA, Ahmad G, Safety Study of a Non-pharmacopial Compound Unani Formulation, Journal of Drug Delivery and Therapeutics. 2019; 9(3):366-368 **http://dx.doi.org/10.22270/jddt.v9i3.2869**

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INTRODUCTION

There are a number of single and compound Unani drugs used in the management of oligospermia and erectile dysfunction. A combination of three drugs including Tukhm-e-konch (*Mucuna pruriens),* Khulanjan *(Alpinia galangal*), and Salabmishri (*Orchis latifolia)* (test drug)in equal amount has been demonstrated to possess significant sex improving effect in experimental studies[1,2] However, this combination has not been studied on safety parameters as mandated by WHO. Therefore present study was undertaken to determine the concentration of aflatoxins, microbial load, pesticide residue and heavy metals in the test drug. Herbs and herbal materials normally carry a large number of bacteria and moulds; often originated in soil or derived from manure. Current practices of harvesting, production, transportation and storage may cause additional contamination and microbial growth. Proliferation of microorganisms may result from failure to control the moisture level of herbal medicines during transportation and storage [3]. Aflatoxin B1, G1, B2 and G2 are fungal secondary toxic metabolites produced by Aspergillums flavus, Aspergillus parasiticus, and Aspergillus nomius. Aflatoxins are the strongest natural carcinogens mainly targeting the liver. The International Agency for Research on Cancer (IARC) has classified aflatoxin B1 in the group 1 as a human carcinogen and aflatoxin G1, B2, and G2 in the group 2B as possible carcinogens[4]. contamination of herbal materials with toxic substances such as arsenic can be attributed to many factors. These include environmental pollution (i.e. contaminated emission from factories, leaded petrol and contaminated water including runoff water which finds its way into rivers. The contamination of the herbal material leads to contamination of products during various stages of the manufacturing[3]. The worldwide consumption of herbal medicines has increased many folds so, it is essential to identify the risk associated with their use by large population. Present study was undertaken to prepare the safety profile ofthe test drug.

MATERIAL AND METHOD

Sample preparation

The crude drugs were taken from Dawakhana Tibbiya Collage A.K.Tibbiya College Aligarh Muslim University, Aligarh. After confirmation of purity and ingredients from pharmacognosy section of Department of Ilmul

Advia. All the ingredients were powdered in an electric grinder separately and mixed altogether thereafter and passed through a mesh no 80. The powdered drug was stored in an air tight container for further studies.

Microbiological Determination Test-

Total Viable Aerobic Count (TVC): Plate count method was used for total aerobic count

Pretreatment of the compound formulation: Compound formulation was dissolved using a suitable method[5] and any antimicrobial property present in the sample was eliminated by dilution and neutralisation method. Dilution was done by Buffer sodium chloride – peptone solution, pH 7.0 (MM1275-500G Himedia Labs, Mumbai, India) was used for diluting the test sample.

Counting of Plate for Bacteria: One ml of pre treated solution was taken and about 15 ml of the liquefied casein soybean digest agar medium in a Petridis of 90 mmdiameter at a temperature not more than 45 ^{0}C Alternativly test sample was spread in a Agar medium by the same solution. Two dishes were prepared which were inverted and incubated at 30-35°C for 48-72 hours unless more reliable count was obtained within a short period of time. The number of colonies formed was calculated and result was calculated using the maximum number of colonies formed in a plate[5].

Test for pesticide residue: The test for the assessment of specific pesticide residues including organochlorine compounds, organo phosphorus compounds and pyrethroids compounds was done using GCMS-MS[6].

Test for Aflatoxins: LCMS-MS was used to determine the different Aflatoxins including B1, G1, B2 and G2,[4].

Test for heavy metals: The concentration of heavy metals including Arsenic, Mercury, Cadmium and Lead[7] was determined with the help of AAS technique.

RESULT AND DISCUSSION

The results have been summarized below in the Tables (1-4):

Table-1: Heavy Metals in NPCU (Non Pharmacopoeial Compound Unani Formulation

S. No	Test Parameter	Result (in mg/kg	LOQ mg/kg)	Permissible limit (mg/kg)
1	Lead (pb)	Not detected	2.50	Not more than 10
2	Mercury (Hg)	Not detected	0.5	Not more than 1
3	Arsenic (As)	Not detected	1.25	Not more than 3
4	Cadmium (Cd)	Not detected	0.25	Not more than 0.3

Table no 2-Microbial Load in NPCU.

S. No	Microbes	Result cfu/gm	Permissible Limit (cfu/gm)
1	Total Bacterial count	6400	Not more than 10^5
2	Total yeast and moulds	300	Not more than 10^3

Table No-3 –Aflatoxins in NPCU

Aflatoxin	Result	LOQ(mg/kg)	Permissible Limit (mg/kg)
Aflatoxin B1(mg/kg)	Not detected	0.001	Not more than 0.5
Aflatoxin G1 (mg/kg)	Not detected	0.001	Not more than 0.5
Aflatoxin B2 (mg/kg)	Not detected	0.001	Not more than 0.1
Aflatoxin G2 (mg/kg)	Not detected	0.001	Not more than 0.1

Table no- 4 -Pesticides Residue: NPCU

S. No	Pesticide Residue	Result	LOQ(mg/kg)	Permissible Limits (mg/kg)
1	Alachor	Not detected	0.02	0.02
2	Aldrin and dieldrin	Not detected	0.04	0.05
3	Azinophos-methyl	Not detected	0.04	1.0
4	Bromoprophylate	Not detected	0.08	3.0
5	Cholordane(sum of cis, trans and oxychlordane	Not detected	0.04	0.05
6	chlorfenvinphos	Not detected	0.04	0.5
7	Chlorpyrifos	Not detected	0.04	0.2
8	Chlorpyrifos-methyl	Not detected	0.04	0.1
9	Cypermethrin (and isomers)	Not detected	0.10	1.0
10	DDT(sum of p,p-DDT,p,p-DDE and p,p-TDE	Not detected	0.04	1.0
11	Deltamethrin	Not detected	0.10	0.5
12	Diazinon	Not detected	0.04	0.5
13	Dichlorvos	Not detected	0.04	1.0
14	Diathiocarbamate (as cs2)	Not detected	0.01	2.0
15	Endosulfan (sum of isomer and Endosulfan sulphate	Not detected	0.04	3.0
16	Endrin	Not detected	0.04	0.05

17	Ethion	Not detected	0.04	2.0
18	Fenitrothion	Not detected	0.04	0.5
19	Fenvalerate	Not detected	0.10	1.5
20	Fonofos	Not detected	0.04	0.05
21	Hepatochlor	Not detected	0.04	0.05
22	Hexachlorobenzene	Not detected	o.o4	0.1
23	Hexachlorocyclohexane isomer	Not detected	0.04	0.3
24	Lindane	Not detected	0.04	0.6
25	Malathion	Not detected	0.04	1.0
26	Methidathion	Not detected	0.04	0.5
27	Parathion	Not detected	0.04	0.5
28	Parathion Methyl	Not detected	0.04	0.5
29	Permethrin	Not detected	0.04	1.0
30	Phosalone	Not detected	0.04	0.1
31	Pipronylbutoxide	Not detected	O.04	3.0
32	Primiphos Methyl	Not detected	0.04	4.0
33	Pyrethrin	Not detected	0.10	3.0
34	Quintozen	Not detected	0.10	1.0

	Test for Microbiology:				
1	Total Bacterial count	6400	..	Not more than 1×10^5cfu/gm	
2	Total Yeast and Mould	300	..	Not more than 1×10	

DISCUSSION AND CONCLUSION

-The findings of the study demonstrated that the test drug is safe as it was found to qualify the criteria of safety as laid down by WHO. The four toxicants were found either present in permissible limits or were not present at all. In Unani system of medicine the crude are though subjected to different procedures of purification and detoxification to make them effective and safe. But a number of objective parameters that have been developed as the attribute of authentication are not taken up to ensure the safety. Since crude drugs undergo the process of cultivation, collection, drying and preservation etc before being procured by the manufacturer therefore there are chances that many unwanted materials, toxicants mainly those present in the soil and atmosphere and that are used to protect the raw material from infection may have occupied a place in the crude drug. Presence of extraneous substance decreases the quality of the drugs and may cause serious side effects when administered for therapeutic purposes. Therefore WHO has identified four important groups of toxic substances that should not be present in any product beyond the specific limit, as they are liable to cause very serious and life threatening side effects..

Therefore it has been made mandatory to ascertain that these agents are not exceeding the permissible limits in a drug sample. The test drug in the present study was found safe because aflatoxin, pesticide residues and heavy metals were not detected at all in the samples whereas the bacterial load was found to be many folds lower than their permissible limits. The findings indicated that the test drug is quite safe and can be used safely in the management of sexual and other diseases.

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