

## Evaluation of acute oral toxicity of Hab-o Shefa in rats

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### A B S T R A C T

**Background and Objective:** Iranian Traditional Medicine (ITM) has a long history in the prevention and treatment of diseases. Clinical uses, side effects, and toxic effects of many singular and compounds were known to scientists of ITM and articular books on toxicology and detoxification of drugs has been written by scientists, but their measurement tools to evaluate chronic toxicity of drugs are limited. Hab-o Shefa is a combination drug which has an important place in Iranian Traditional Medicine to cure drug addiction. According to the attention of people to traditional medicine and expanding the use of natural drugs, and also, more attention to treatment of addicts, clinical studies on its toxicology are required. However, we decided to do oral toxicity study of this combination in rats.

**Materials and Methods:** Acute oral toxicity of Hab-o Shefa in male Wistar rats was evaluated using doses of 200, 500, 1500, 2000, 3000, 4000, and 5000 mg per kg of body weight. Protocol that we used to define acute toxicity and determine LD50 of Hab-o Shefa was based on the method that proposed by Mr. Smith and colleagues (1960) and the changes to it by Mr. Van Dan Howell in 1990.

**Results and Conclusion:** The results showed apparently no toxicity and mortality in rats. Histopathological studies of the vital organs of rats at these dosages did not show any histological abnormalities.

### 1. Introduction

Addiction is a phenomenon that has existed in human society for a long time. Nowadays, despite scientific advances, and increasing public awareness, addiction is still under development and every year many people are suffering from it (1). Although current therapies are effective in cases, but they are not able to complete treatment of addiction. So, the global movement is widely towards Traditional Medicine Schools (2). ITM has a long history in the prevention and treatment of diseases. Clinical uses, side effects and toxic effects of many singular and compounds were known to scientists of ITM and articular books on toxicology and

detoxification of drugs has been written by scientists, but their measurement tools to evaluate chronic toxicity of drugs has been limited (3). Toxicological studies before clinical trial for herbal and natural drugs is scientifically reasonable for taking these drugs widely and it proves the efficacy and safety of them (2). Hab-o Shefa is the combination of *Datura seeds (Datura stramonium)*, ginger rhizome (*Zingiber officinalis*), Rhubarb root (*Rheum palmatum*), and Arabic gum (*Acacia arabica*). In authoritative textbook of ITM, this combination has been introduced as a viable alternative to opium addiction. Also, it cures acute and chronic pain and cough and numerous other cases (4-7, 9). In

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reviewing the articles, we did not find any report on the assessment of toxicity of this compound. So, we decided to examine the acute toxicity of this drug.

## 2. Materials and Methods

Hab-o Shafa is one of the combination drugs in ITM that is composed of *Datura* seeds (*Datura stramonium*), ginger rhizome (*Zingiber officinalis*), Rhubarb root (*Rheum palmatum*), and Arabic gum (*Acacia arabica*). The raw materials of this combination are purchased from market of medicinal plants (Attari) of Iran and it was prepared in Traditional Medicine laboratory of Shahed University. The recommended dose in ITM books as an alternative to opium addiction was 1.6 grams/day (4-8).

### 2.1. Animals

Male Wistar rats with an average weight of 116±22 g were purchased from Pasteur Institute of Iran and they were maintained at Pharmacology laboratory (School of Pharmacy, Tehran University of Medical Sciences) and with standard conditions and normal feeding (10). After ensuring their health, we used them for pre-test and test groups in toxicology lab.

### 2.2. Experimental procedure

The protocol that we used to define acute toxicity and determine LD50 of Hab-o Shefa was based

on the method that was proposed by Mr. Smith and colleagues (1960) and some changes by Mr. Van Dan Howell in 1990 (11-16). In this method, at first we did a pre-test. In this exam, rats were gavage-fed with different doses up to 3000 mg per kg of Hab-o Shefa, by geometric method and were monitored for 24 hours. If death was observed in animals for that dose, we considered the dose before it as the middle dose. Then, we multiplied them at the rate of 2.3 and 3.2. At least 5 single doses were gavage-fed in the test groups. Therefore, concentrations of Hab-o Shefa (200, 500, 1500, 2000, 3000, 4000, and 5000 mg per kg) with saline was prepared in the laboratory. The animals were divided into four groups, the control group received only saline in a standard volume. The other three groups received doses of medication as a single dose and then they were monitored for 14 days and control parameters including animal's body hair, the skin, subcutaneous edema, abdominal distension, eyes dullness, eyes opacities, pupil diameter, ptosis, color and consistency of the feces, wetness or soiling of the perineum, condition of teeth, breathing and walking, the amount of food and water intake and body weight and mortality were daily recorded (17-22). Finally, the vital organs such as the spleen, lungs, liver and kidneys of two animals in each group were sampled and sent to the pathology laboratory for preparing paraffin sections and stained with Hematoxylin and Eosin staining (23-25).

**Table 1.** The results of measured parameters in rats.

No	Parameters	Observation
1	Condition of the hair	Normal
2	Skin	Normal
3	Subcutaneous swellings	Nil
4	Abdominal distension	Nil
5	Eyes dullness	Nil
6	Eyes opacities	Nil
7	Pupil diameter	Normal
8	Ptosis	Nil
9	Color & consistency of the feces	Normal
10	Wetness or soiling of the perineum	Nil
11	Condition of teeth	Normal
12	Breathing abnormalities	Nil
13	Gait	Normal

### 3. Results & Discussion

In pre-testing exams, rats were monitored for 24 hours and during this time there was no mortality. In the test groups, as can be seen in Table 1, rats that received the drug as a single dose by gavage, were monitored for 14 days and during this period, daily review of control parameters and no changes were observed. Also, during this study, significant weight loss which represents drug side effects and mortality was not observed. In pathological studies of animal tissues, no pathologic changes were reported for liver, kidney, pancreas, and lung tissues. Due to the lack of changes in the control parameters measured in this study and the lack of weight changes and mortality of animals, even at the highest dose of 5000 mg /kg, Hab-o Shafa can be a safe drug and it can be used in human clinical trials with its recommended dosage in ITM book.

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