Reviewer’s report

Title: Acute and sub-acute toxicity study of a Pakistani polyherbal formulation

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Reviewer: Ian Musgrave

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This is an interesting study of the toxicity of a polyherbal remedy. Unfortunately there are numerous issues which need to be attended to.

There is no explanation given for why mice are used for acute toxicity then rats for sub chronic, why not the same species throughout? Also, in the discussion it reads as if only rats were used.

There is no citation to show that the preparation being studied is effective in liver disorders.

Page 4, line 53: "After the arrival of 'medical science' the phytotherapy was given the grade of alternative therapy." This is not actually true. Some phytotherapies (fox glove, cinchona) were superseded because the pure compounds (digitalis, quinine) could be given reliable and accurately, others (salicylin in willow bark, yohimbine) were speeded by more effective compounds that were produced (acetylsalicylic acid, beta blockers). Some phyotherapies are alternative medicines, but many became feedstocks for purified chemicals. Why is medical science in quotes?

Page 4, line 54: "Herbal therapy encompasses … Homeopathic." Homeopathic medicine is not herbal medicine, as there is no trace of the original compounds in the homeopathic medicines.

Problems with references:

Page 4, line 60: "a number of botanical drugs, have proved to be very efficient in curing sicknesses [4]." Reference 4, "Subacute toxicity and stability of Soshiho-tang, a traditional herbal formula, in Sprague-Dawley rats" does not support this statement, but is a toxicological study of one herbal therapy.

Page 4, line 64: "These combinations are employed for the betterment of various chronic disorders [6]" Reference 6, "Acute and subacute toxicity studies on the polyherbal antidiabetic formulation Diakyur in experimental animal models" does not support this (and should be reference 7, as it supports the following sentence).

Page 4, line 71: "In addition to this, conventional people and even still certain physicians invoke the usage of medicinal 72 and curative herbs to aid the medication therapy for better clinical outcomes [8]" is not supported by reference 8, "Evaluation of acute and sub-chronic oral toxicity study of baker cleansers bitters - a polyherbal drug on experimental rats".
Reference 23 is in the wrong format and has no journal, volume of page number.

Statistics: The data are expressed as mean and standard error of the mean, not "Values are expressed as standard error of mean" as is used throughout.

"*** represents highly significant p<0.01" highly significant is not an appropriate statistical term "*** represents significance of p<0.01" is more appropriate.

Interpretation: Page 11, line 192 "This effect indicates that the formulation considerably decrease the raised liver enzymes" the control values for ALT and AST are within the reference ranges of normal rats, these values are not raised.

What is the normal dose of Hab e Kabad Noshadri for an adult human? How does this compare to the doses in this study? As the preparation is to be given to people with liver disease, the adverse liver effects must warrant more caution than suggested in this paper.

Minor issues:

(these are examples only, there are too many issues to be individually listed)

Page 2, line 1: "Acute and sub-acute toxicity study of Pakistani polyherbal formulation" would be better as "Acute and sub-acute toxicity study of a Pakistani polyherbal formulation"

Page 3 line 30: "methodology, has a wide spread to people at risk of contracting." Risk of contracting what?

Page 3, line 31: "The aim of study was to assess the acute and sub-acute toxicity of polyherbal formulation" is better as "The aim of this study was to assess the acute and sub-acute toxicity of the polyherbal formulation"

Page 3, line 32: "In acute study, single dose of 2000mg/kg was administered to the mice and were observed for physical symptoms and behavioral changes for 72 hrs" would be better as "In the acute arm of the study, a single dose of 2000mg/kg was administered to Swiss Albino mice which were observed for physical symptoms and behavioral changes for 72 hrs".

Page 3, line 33: "In sub-acute toxicity studies repeated doses of polyherbal preparation was administered in rats of both genders, separately." Is better as "In the sub-acute toxicity studies repeated doses of the polyherbal preparation was administered to rats of both genders, separately."

Page 3, line 36: "On 28th day of experiment, blood sampling of animals were done" is better as "On the 28th day of experiment, blood sampling of animals was done"

Page 4, line 50: "Herbal medicines are focused as the popular therapies to treat diseases by the largest group of world population" do the authors mean something like "For most of the world's
population, herbal medicines are the most popular form of therapy”. For many, it is the only available or affordable therapy.

Page 4, line 51: They have accomplished widespread appropriateness as medicinal agents.” I am uncertain as to what this sentence means.

Page 4, line 52: "Before 1800, when medicinal therapy was introduced in the scientific era, the herbal therapy was the only obvious choice" is better as "Before 1800, when science-based medicinal therapy began to be introduced, herbal therapy was the only available choice” (this is not actually true, mineral drugs such as mercury were in use since medieval times, and the use of sulphur as a medicine dates back to classical Greece).

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
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No

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