Reviewer's report

Title: Anti Hyperglycemic and Renal Protective Activities of Terminalia chebula Seed Powder Chloroform Extract in Streptozotocin Induced Diabetic Rats

Version: 1 Date: 10 June 2005

Reviewer: T Dunning

Reviewer's report:

General

There are a number of typographical errors, inconsistencies, missing words and structural issues that require attention.

Specific comments

Title
The title is appropriate and reflects the contents of the paper. However, “properties” may be a more appropriate term than “activities”.

Abstract
The abstract requires some revision to improve the flow of the information and to more accurately reflect the information reported in the text.
The aims/hypothesis need to be stated.
The methods require clarification for example how blood glucose levels were determined is not clear.
The phases of the study require clarification. “Acute” usually refers to a hospital admission and “chronic” to incurable diseases. “Short” or “immediate” and “long term” effects may be more appropriate.
Were baseline urine samples collected and compared with the 8 week samples? Is 8 weeks sufficient time to show a change?
The method describes rats but results section discusses “diabetic rabbits”—clarify what happened to the rats.
In the main text T chebula was compared with glibenclamide and glipizide.

Introduction
The introduction is very brief. More discussion about diabetes, its complications, conventional management and other herbs with hypoglycaemic properties such as Momordica charantia, Opuntia streptocantha, Trigonella foenum graceum, should be included.
Discuss issues concerning the standardisation and purity of herbal therapies and other safety issues would also enhance the paper.
The information detailing the indications for use of T chebula could be presented in a table.
The sentence “It has also claimed to be useful in diabetes” is vague. Clarify what “useful” means in this context.
The aims/hypothesis need to be stated.
It is not clear whether the aim was to establish hypoglycaemic effect and/or compare T chebula with conventional oral hypoglycaemic agents, or whether it was a dose finding trial.
Clearly stating the aims of the study and outcomes measured would help clarify these issues.

Materials and methods
An appropriate method appears to have been used although the aims/hypothesis was not clearly stated. The study aims are very important in determining the most appropriate method to use.
The information could be reorganised to make this section easier to read. For example indicate the study consisted of two parts: a) acute and b) chronic. These terms need to be defined for the purpose of the paper. “Acute” often refers to care in hospital or curable conditions and chronic to incurable diseases such as diabetes whereas the context here appears to be the immediate effect of the T chebula extract after a fast (acute) and the longer term effect (after 28 days) of treatment with T chebula extract.

2.1 Details about how the plant material was verified could be included, for example was a plant classification system such as the International Code of Botanical Nomenclature used?

2.2 Suggesting products were a gift could represent a conflict of interest. It is preferable to use phrases such as “supplied by”.

Specify whether “Dr Reddy’s laboratories” is the correct name.

2.3 Clarify that there were eight groups with five rats in each group (n=40).

Clarify whether “Dr Reddy’s laboratories” is the correct name.

2.3.1 Note previous comments about terminology.

The section would be easier to follow if the study groups and treatment mode were listed or presented in a table. Currently it is not clear whether all the rats in groups 1–3 were given incremental doses of T chebula commencing at 100 mg/kg and increasing to 200 then 300 mg/kg or whether group 1 had 100 mg/kg, group 2, 200 mg/kg and group 3, 300 mg/kg.

Clarify what “appropriate volumes of vehicle” means.

2.3.2 Note earlier suggestions about terminology “chronic”, “standard” and presentation of the material.

Clarify the dose intervals for the T chebula, and glibenclamide. Glibenclamide is a long acting agent; therefore a daily dose would be indicated.

2.3.3 Clarify whether blood glucose monitoring continued for 8 weeks (32 days) or whether this aspect of the study only measured kidney function.

Indicate how 28 days was chosen as the end point of the chronic study.

Clarify what “standard diagnostic kits were”. Was the albumin creatinine ratio estimated? Was microalbumin measured in urine or was it albumin? Microalbuminuria precedes albumin and is an early marker of renal disease. Were kidney pathology, morphology and blood flow examined? In the early stages of diabetic nephropathy the kidney is enlarged, but reduces to some extent when treatment is initiated and the blood glucose normalises. It may be premature to claim renal protective activity for the T chebula without more information about the mechanisms of action. These issues need to be discussed in the discussion.

The abstract and results discuss urine tests where blood samples are discussed in this section.

Clarify the discrepancy.
Results and discussion
In paragraph 1, sentence 7 a dose of 150 mg/kg is reported but this dose is not described in the method.
Note suggested terminology.
More discussion about the clinical relevance of the study is needed and whether rat data can be applied to humans.
Clarify why such an old reference, 1986, is quoted to support the need for “more appropriate therapies” given the enormous advances in oral hypoglycaemic agents and insulin in recent years.
Discuss how herbal medicines might be used in place of or with these agents and the safety issues that arise when the herbs are used with conventional medicine.
Are the researchers appropriately state the need to identify the “active principles” responsible for the hypoglycaemic effects and their mechanisms of action.
Clarify what earlier results the study substantiated.
Note comments about the effects on renal function.
Include conclusions and discuss the limitations of the study.

References
Note references 11, 12 and 13 are very old and more up-to-date references exist and should be used.

Tables and figures
The tables and figures appropriately summarise the results.
Table 1 is difficult to interpret. Clarify that n=5 means five rats per group (also table 2).
Clarify that row two refers to time in hours.
Clarify diabetic controls refers to blood glucose level.
Write out “figure” in full, figures 1 and 2.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

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Discretionary Revisions (which the author can choose to ignore)