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## Hypoglycemic effect of YXK12 (polyherbal product) in normal rats

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### ABSTRACT

Diabetes mellitus [DM] is a chronic metabolic disorder that continues to present a major world wide health problem. Many herbal products have been used in an attempt to cure or control DM, since ages. Numerous herbal drugs like *Momordica charantia*, *Tinospora cordifolia*, *Terminalia cattapa*, *Melia azadirachta* and *Syzygium cumini* have been used by people of various cultures to treat diabetes. YXK12 is a recently introduced, commercially available, polyherbal product being recommended for use in diabetic patients. As no data is available on the safety and efficacy, of this polyherbal combination, the present study was undertaken to study and evaluate the hypoglycemic property of this polyherbal product in normal rats. Hypoglycemic effects of two doses of YXK12 [1000 mg/kg and 2000 mg/kg] was tested in Wistar rats in two groups of six animals each and the results were statistically compared with the results of Tween 80 [vehicle] and Glibenclamide [standard drug], also from two groups of six animals each. Significant hypoglycemic effects [P<001] were observed only in higher dose [2000 mg/kg] in normal rats. The current study has demonstrated hypoglycemic activity only in very high doses in normal rats. This dose [2000 mg/kg in rats] if converted to human dose is equivalent to highest human dose recommended. As lower doses have not demonstrated any hypoglycemic activity, lower doses in humans needs to be evaluated.

**Key words:** YXK12, hypoglycemia, normal rats.

### INTRODUCTION

Diabetes mellitus [DM] is a chronic metabolic disorder that continues to present a major world wide health problem. Estimates predict that 300 million people will suffer from diabetes mellitus by 2025. The prevalence in India was found to be 2-4% in rural areas and 4-11% in urban dwellers<sup>1</sup>. Many herbal products, several metals and minerals have been used in an attempt to cure or control DM, since ages. Plants have been an exemplary source of drugs and many of the currently available drugs have been directly or indirectly derived from them<sup>2</sup>. Numerous herbal drugs like *Momordica charantia*, *Tinospora cordifolia*, *Terminalia cattapa*, *Melia azadirachta* and *Syzygium cumini* have been used by people of various cultures to treat diabetes. Similarly, Ayurveda, an ancient Indian system of medicine, mentions several plants that are useful in the correction of metabolic disorders such as diabetes mellitus<sup>3</sup>. Although some of these plants have a great reputation in Ayurveda, the indigenous Indian system of medicine, many remain to be scientifically established<sup>4,6</sup>. 'YXK12' [not a brand name] is a recently introduced, commercially available, polyherbal product being recommended for use in diabetic patients. Ingredients of the product as published by the manufacturer are [in 5ml] – *Phyllanthus emblica* 80mg, *Terminalia chebula* 80mg, *Terminalia bellerica* 80mg, *Eugenia jambolina* 80mg, *Picrorhiza kurrora* 80mg, *Swertia chirata* 80mg, *Tinospora cordifolia* 80mg, *Gymnema synvestol* 80mg, *Momordica charantia* 80mg, *Curavola longa* 80mg, *Salacia chinese* 120mg, *Melia azadirachta* 80mg. Different polyherbal products with three or four of these ingredients are already tested and marketed in India. But probably a polyherbal product with 12 ingredients, all with hypoglycemic activity, has not been marketed so far. No data is available in literature on the safety and efficacy, of this polyherbal combination. Hence, the present study was undertaken to study and evaluate the hypoglycemic property of this polyherbal product in normal rats.

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### MATERIALS AND METHODS

**Test drug:** YXK12 [Commercial name changed] was purchased from local pharmacy outlets taking care to see that all the requirements of the drug came from the same batch of manufacturing process.

**Study setting:** Animal house of Department of Pharmacology, Kasturba Medical College (KMC), Mangalore.

**Animals:** Adult albino Wistar rats of either sex, weighing 150-200g, housed in standard cages under standard conditions in the animal house<sup>7</sup>. Fasted animals were deprived of food for 18 hours, but had free access to water<sup>8</sup>. The study was approved by the institutional ethics and animal committee, KMC, Mangalore.

**Experimental design:** Method described by Vijay S et.al was followed<sup>8</sup>. Fasted animals were divided into four groups of six animals each. Sub-groups of animals included control group [Tween 80], positive control group [Glibenclamide] and two groups where test drug YXK12 was used in two increasing doses (1000 & 2000 mg/kg). Drugs were administered 18hrs after fasting, orally with the help of stomach tube. Fasting blood glucose [FBS] level was monitored in blood samples collected from tail vein using a glucometer before administration of the drugs. It was again measured two hours after administration of the drug.

**Statistical analysis:** One way analysis of variance was used to compare Blood glucose levels in various groups, followed by Dunnet's multiple comparison tests using SPSS package version 10. P<0.05 was considered statistically significant.

### RESULTS:

Table 1 shows the effect of drugs on fasting blood glucose levels in normal rats. Percentage of decrease of blood sugar levels after administration of drugs in various groups were calculated and compared for statistical significance. Blood sugar levels fell among rats belonging to control group by

**Table 1. Effect of YXK12 on blood glucose levels of normal rats**

Groups	Treatment	Dose	Blood glucose levels (mg/dL)		Percentage decrease
			Pre-treatment	Post-treatment	
Vehicle Control	Tween 80	0.5ml/kg	74.66±4.91	72.16±4.82	3.40±0.84
Positive control	Glibenclamide	0.5mg/kg	59.00±2.72	52.8±2.46	10.45±0.47**
Test drug lower dose	YXK12	1000mg/kg	68.66±2.75	66.5±2.41	3.08±0.49
Test drug higher dose	YXK12	2000mg/kg	65.50±2.14	61.33±2.10	6.38±0.59*

3.40%±0.84. Fall of blood sugar levels in Glibenclamide group was 10.45±0.47%. Fall of blood sugar level among two test drug groups of YXK12 was 3.08±0.49% [1000 mg/kg] and 6.38±0.59% [2000mg/kg]. Only the hypoglycemic effects of Glibenclamide (P<0.001) and YXK12 2000mg/kg (P<0.015) were found to be statistically significant. Hypoglycemic effect of YXK12 [2000 mg/kg] was less than that of Glibenclamide. Blood sugar lowering effects of YXK12 in the lower dose of 1000mg/kg was found statistically not significant when compared to control group, P value, being 0.487.

## DISCUSSION

Many combinations of herbs, polyherbal preparations like *Byesukar*<sup>9</sup>, *Hachimi-jio-gan*<sup>10</sup>, *Dianex*<sup>11</sup>, have been successfully tested in laboratories for hypoglycemic properties. Many of the ingredients like *Phyllanthus emblica*<sup>12</sup>, *Terminalia chebula*<sup>13</sup>, *Terminalia bellerica*<sup>4</sup>, *Eugenia jambolina*<sup>14</sup>, *Picrorhiza kurrora*<sup>15</sup>, *Swertia chirata*<sup>16</sup>, *Tinospora cordifolia*<sup>17</sup>, of the preparation [YXK12] being tested in this study are already successfully tested in animals for anti diabetic activity. However no data is available about the hypoglycemic effects of the combination of herbs found in this test drug. In the current study test drug [YXK12] was administered in two doses (1000 mg/kg and 2000 mg/kg) to normal rats. Statistically significant hypoglycemic effect of this polyherbal product YXK12 was demonstrated only in the higher of the two doses, in this study. At a dose of 1000 mg/kg, which is equivalent to high doses recommended in humans with severe diabetes, no significant hypoglycemic effect was observed. Only a higher dose of YXK12 [2000 mg/kg] has shown the ability to lower blood glucose levels, significantly, in normal rats. Another polyherbal product, Triphala, which contains extracts of some of the herbs found in YXK12 [*Terminalia chebula*, *Terminalia bellerica*, *Emblica officinalis*], has demonstrated hypoglycemic activity in experimental animals at a low dose of 100 mg/kg<sup>8</sup>. There is a possibility that at lower doses of YXK12 has antidiabetic effect through extra pancreatic actions, in which case it may not show substantial hypoglycemia. The reason why YXK12 shows hypoglycaemic activity only at very high doses requires further evaluation. Drug interactions may also be a factor. However, these hypothesis need to be tested in further studies using diabetic animals.

## CONCLUSION

This product [YXK12], which is a combination of 12 herbs, is recommended by the manufacturer in both Type 1 and Type 2 diabetes. Current study has demonstrated hypoglycemic activity only in very high doses in

normal rats. This dose [2000mg/kg in rats] if converted to human dose is equivalent to highest human dose recommended for diabetic patients. As lower doses have not demonstrated any hypoglycemic activity, lower doses recommended in humans needs to be evaluated. Further evaluation in diabetic rats may also yield useful information

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