



EFFECT OF VASANT KUSUMAKAR RAS ON BLOOD GLUCOSE LEVELS OF FASTED NORMOGLYCEMIC AND ORAL GLUCOSE INDUCED HYPERGLYCEMIC SD RATS

Ayurveda

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ABSTRACT

Vasant Kusumakar Ras is an herbo-mineral formulation known for its anti-diabetic activity. Ayurvedic literature describes Vasant Kusumakar Ras to possess Pramehgana (anti-diabetic), properties. The objective of the current study is to investigate the hypoglycaemic effect of Vasant Kusumakar Ras in fasted normoglycemic and antihyperglycemic effect in oral glucose induced hyperglycemic rats. The male and female Sprague Dawley rats were randomized in to 3 groups based on the bodyweight. One group serves as control which was treated with vehicle and other 2 groups of animals were treated with Vasant Kusumakar Ras 25 mg/kg and Glibenclamide 10 mg/kg respectively. The duration of the drug treatment in hypoglycaemic study was for a period of 7 days. The blood glucose levels were analysed in fasted normoglycemic animals on 1st, 3rd & 7th day, prior as well as post 01 hr of drug administration. Similarly, the oral glucose tolerance test (OGTT) was carried out on day 8th by challenging the same rats with oral glucose (2 g/kg). The drugs were administered simultaneously the blood glucose was analysed at 0th, 1st, 2nd and 3rd Hr of post drug treatment. During the hypoglycaemic study on day 7th, the Vasant Kusumakar Ras treatment significantly reduced the blood glucose levels ($p < 0.05$). Similarly, during the OGTT the test drug reversed the hyperglycemia induced by oral glucose at 2nd and 3rd Hr intervals. From this study it was concluded that the Ayurvedic formulation Vasant Kusumakar Ras possess significant hypoglycaemic activity in fasted normoglycemic and antihyperglycemic effect in glucose induced hyperglycemic rats. This may suggest the ethno pharmacological use of Vasant Kusumakar Ras to reduce the hypoglycaemic episodes in diabetic and hyperglycemic non diabetic subjects.

KEYWORDS

Hypoglycaemia, VK Ras, OGTT, Sprague Dawley, Normoglycemic, Diabetic

INTRODUCTION

Vasant Kusumakar Ras, is an herbo mineral preparation used widely in the treatment of diabetes.^[1] Its ingredients are Swarna Bhasma (Bhasma of Gold), Rajata Bhasma (Bhasma of Silver), Vanga Bhasma (Tin Calx), Ekagunasindhoora (Mercury), Naga Bhasma (Lead Calx), Loha Bhasma (Bhasma of Iron), Abhraka Bhasma (Purified and processed Mica), Praval Bhasma (Bhasma of Coral), Mukta Bhasma (Bhasma of Pearl).^[2] These ingredients will be processed with Godugdha (Cow milk), Ikshuras (sugar cane juice), Vasa pataras (Adathoda leaves decoction), Chandana ras (Sandal wood decoction), Usiraras (Vetiver roots decoction), Hrивeraras (Black Vetiver roots decoction), Haridraras (Turmeric decoction), Rambha ras (Banana rhizome), Padma Pushpa ras (Lotus flower juice), Jatipushparas (Jasmine flower juice) and finally kasturi (musk) will be added. It is used in the treatment of poly urea, memory loss, cough, diseases related to urinary tract, cardiac and hepatic disorders.^[3]

Acute oral toxicity with Vasant Kusumakar Ras neither showed signs of toxicity, nor mortality in Swiss albino mice at a dose of 2.5, 5 and 7g/kg body weight. Similar results were observed with single dose intra peritoneal administration of Vasant Kusumakar Ras at dose 500 mg/kg body weight. Chronic 180 days repeated oral dose toxicity evaluation of Vasant Kusumakar Ras with a dose of 20, 100 and 300 mg/kg bd.wt showed no significant signs of toxicity. Incidental findings in this study are not treatment related.^[4]

Vasant Kusumakar Ras is a herbo-mineral formulation known for anti-diabetic activity. Ayurvedic literature describes Vasant Kusumakar Ras to possess *Pramehgana* (anti-diabetic), properties. In a clinical study, Vasant Kusumakar Ras along with Phalayrikadi was effectively used in the treatment of Prameha.^[5]

MATERIALS AND METHODS:

Animals

The study was performed in male and female *Spargie Dawley* rats. Animals were procured from the small animal veterinary breeding station, Mannuthy, Thrissur, Kerala. The study was conducted as per the recommendations of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) guidelines for Laboratory Animal Facility after approval of Institutional Animal Ethics Committee (IAEC/NARIP/2018-19/02), NARIP, Cheruthuruthy.

Procurement Of Drug And Its Composition

Vasant Kusumakar Ras, an Ayurvedic drug procured from M/S. Dhootapapeshwar Ltd, Mumbai, India (Batch No. P200900133; MFG. LIC. Number: AYU-150; Date of Manufacture: 09/2020 and Date of Expiry: 08/2025). The drugs were kept under room temperature and humidity of $52 \pm 10\%$ RH until experiment gets completed.

Each 1 gram powder of Vasant Kusumakar Ras contains 4.310 mg of Suvarna (Svarna) Bhasma, 4.310 mg of Rajata Bhasma, 6.465 mg of Vanga Bhasma, 6.465 mg of Naga Bhasma, 6.465 mg of Kanta Loha Bhasma, 8.620 mg Rasasindoor, 8.620 mg of Abhraka Bhasma, 8.620 mg Praval Bhasma, 8.620 mg Moutik Bhasma (Mukta) processed in godugdha, ikshu (*Saccharum Officinarum*), stems swaras, vasa (*Adatoda Vasaka*), leaf swaras, chandhana (shveta) (*Sanathum Album*) Heart wood Kwath, Ushira (*Vetiveria Zizanioides*), fibrous root Kwath, Rheebera (*Pavonia Odorata*) fibrous root Kwath, Haridra (*Curcuma Longa*) Rhizome Kwath, Kadali (*Musa Paradisiaca*) Rhizome Swaras, Kamala (*Nelumbium Speciosum*) flower Swaras, Jati (*Jasminium Officinale*) q.s

Environment, Housing Acclimatization

Animals are housed individually in rat cages with free access to food and water ad. libitum. Each cage was identified with cage card, which displayed with study number, cage number, sex, duration of study and animal identification number. Animals were acclimatized for 1 week before initiating the study.

Grouping and randomization of animals

The male and female animals were randomized based on the body weight and distributed in to three groups, each group consisted of 6 animals (03 male + 03 female).

Group-I: Control

Group-II: Vasant Kusumakar Ras (25 mg/kg)

Group-III: Glibenclamide (10 mg/kg)

Effects Of Vasant Kusumakar Ras On Blood Glucose Levels Of Fasted Normoglycemic Rats

The overnight fasted rats were treated with respective vehicle (control), test drug (25 mg/kg of VK Ras) and Glibenclamide (10 mg/kg). The treatment was continued for a period of 7 days. On day 1, 3 & 7 prior and post 01 hr of drug administration the blood glucose was analysed with accucheck blood glucose monitoring strips by puncturing the tail vein.^[5]

Effects of Vasant Kusumakar Ras on hyperglycemia during OGTT

The rats mentioned in the previous section was used for oral glucose tolerance test (OGTT) which was carried on 8th day. The animals were treated with the glucose (2 g / kg) orally. drugs were given post glucose loading and blood was withdrawn by puncturing the tail vein. The analysis of glucose was done at 0th, 1st, 2nd and 3rd hr using accucheck blood glucose monitoring strips.^[5]

Statistical Analysis

Results obtained from the present study were expressed as Mean $\pm$ SEM. Data was subjected to statistical analysis through one way analysis of variance (ANOVA) with multiple comparisons using sidaks test by using Graph pad prism software. $p < 0.05$ was considered as statistically significant.

RESULTS

Effects Of Vasant Kusumakar Ras On Blood Glucose Levels Of Fasted Normoglycemic Rats

The blood glucose levels of all the groups were checked on 1st, 3rd and 7th day at 0th Hr (prior to drug administration) and 1st Hr (post drug administration). No significant changes in blood glucose levels were observed prior to drug administration (0th Hr) in VK Ras and glibenclamide treated as compared to control animals on Day 1, 3 and 7 ($p > 0.05$). Similarly, no significant changes in glucose levels post 1 Hr of VK Ras treatment ($p > 0.05$). However, on 7th day the VK Ras treated animals had shown significant decrease in blood glucose levels as compared to control animals ($p < 0.05$). Post drug administration significant hypoglycaemia observed in glibenclamide treated animals on day 1 ($p < 0.01$), day 3 ($p < 0.05$) & day 7 ($p < 0.0001$). [Table 01 & Fig.1]

Table 1: Blood Glucose Levels (mg/dL) Of Fasted Normoglycemic Rats

Day and Hr	Control	VK Ras	Glibenclamide
1st day 0hr	108 $\pm$ 08	101 $\pm$ 06 ^{ns}	98 $\pm$ 05 ^{ns}
1st day 1 hr	97 $\pm$ 06	81 $\pm$ 12 ^{ns}	54 $\pm$ 06 ^{**}
3rd day 0hr	102 $\pm$ 05	94 $\pm$ 05 ^{ns}	88 $\pm$ 03 ^{ns}
3rd day 1 hr	86 $\pm$ 05	68 $\pm$ 08 ^{ns}	61 $\pm$ 02 [*]
7th day 0hr	103 $\pm$ 07	82 $\pm$ 08 ^{ns}	79 $\pm$ 05 ^{ns}
7th day 1 hr	91 $\pm$ 06	65 $\pm$ 06 [*]	45 $\pm$ 04 ^{****}

[Values are expressed as mean $\pm$ SEM of 3 rats] * $p < 0.05$; **** $p < 0.0001$; ^{ns}-Non significant]. Data was subjected to analysis through one way ANOVA with sidaks multiple comparison test. VK Ras and Glibenclamide were compared with control.

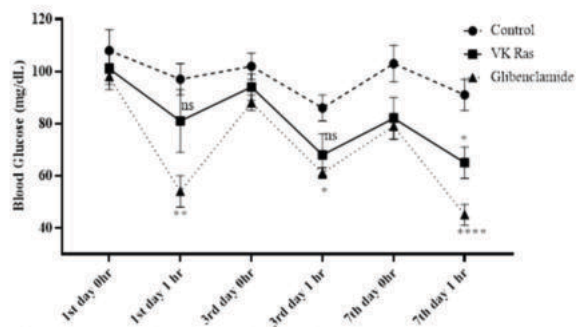


Fig.01. Effects of VK Ras on blood glucose levels (mg/dL) of fasted normoglycemic rats

Effects of Vasant Kusumakar Ras on hyperglycemia during OGTT

Immediately after glucose feeding the drugs were administered to respective groups. The change in glucose levels were observed at 0th, 1st, 2nd and 3rd Hr.

No significant change in blood glucose at 1 hr when compared to the control blood glucose levels ($p > 0.05$). However, post 2 to 3 hrs of VK Ras treatment significant decline in blood glucose levels were observed ($p < 0.05$). [Table 02 & Fig.02]

Table 02: Blood glucose levels (mg/dl) during OGTT

Hr	Control	VK Ras	Glibenclamide
0hr	90 $\pm$ 07	92 $\pm$ 03	72 $\pm$ 10
1st hr	141 $\pm$ 08	130 $\pm$ 02 ^{ns}	102 $\pm$ 13 [*]
2nd hr	108 $\pm$ 06	85 $\pm$ 06 [*]	69 $\pm$ 04 ^{***}

3rd hr	94 $\pm$ 06	70 $\pm$ 06 [*]	60 $\pm$ 05 ^{**}
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[Values are expressed as mean $\pm$ SEM of 3 rats] $p < 0.05$; $p < 0.01$; $p < 0.001$; ^{ns}-Non significant]. Data was subjected to analysis through one way ANOVA with sidaks multiple comparison test. VK Ras and Glibenclamide were compared with control.

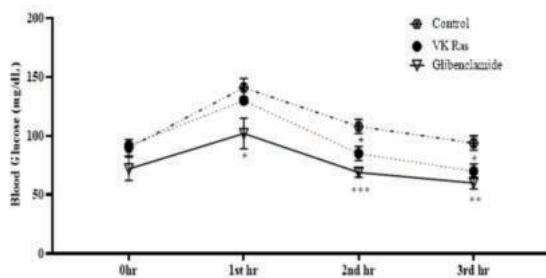


Fig.02. Blood glucose levels during OGTT

DISCUSSION

Ayurveda is an Indian traditional medicinal practice with roots tracing back to 2000 BC. According to Ayurveda, striking an equilibrium between the doshas corresponds to good health and mental state of being. The main medicinal products used in Ayurveda derived from plants, minerals, metal, marine and animal-based products. The patronage towards ayurvedic therapies is snowballing due to its effectiveness as well as safety. World Health Organization begun to understand the benefits of traditional medicines in the late 1970s and initiated to promote the concepts of Ayurveda.^[6] The mentioning of Diabetes mellitus or Madhumeha as it is known to the ancient Indian physicians can be found in classical texts such as *Charakasamhita*, *Sushrutasamhita*, *Ashtanga sangraha*, *Madhava nidana* and *Yoga ratnakara*. The causes of diabetes are well described as consumption of *guru* (heavy to digest) and *lavana* (salty) *ahara*, *Asyasukha* (sedentary life style), *atinidra* (excess sleep), *avyayama* (lack of exercise), *achinta* (lack of mental exercise) and abstaining from *samshodhana* (purification) therapy.^[7] Ayurvedic preparations containing shilajit, turmeric, neem, coccinea indica, amalaki, triphala, bitter gourd, rose apple, leaves of bilva, cinnamon, gymnema, fenugreek, bay leaf and aloe vera can be used for the treatment of madhumeha.^[8] The most notable ayurvedic preparations for the treatment of diabetes mellitus or madhumeha are 'Vasant Kusumakar Ras' and 'Chandraprabhavati'.

Vasant Kusumakar Ras is a herbo-mineral formulation known for anti-diabetic activity. It contains, *Svarna*, *Rajata*, *Vanga*, *Naga*, *Kantaloha*, *Abhraka*, *Pravala* and *Mouthika Bhasmas* along with herbal components such as *Saccharum officinarum*, *Adhatodavasisa*, *Santalum album*, *Vetiveriazaniodes*, *Pavonia odorata*, *Curcuma longa*, *Musa paradisiaca*, *Nelubium speciosum* and *Jasminum officinale*. Ayurvedic literature describes Vasant Kusumakar Ras to possess *Pramehgana* (anti-diabetic), *Ojovardhaka* and *Rasayana* (improves immunity, rejuvenator) properties and thus can have a protective role in diabetes.^[9] Studies have shown that Vasant Kusumakar Ras prevents the development of diabetic retinopathy in rats by inhibiting retinal aldose reductase and vascular endothelial growth factor (VEGF) expression.^[10]

Oxidative stress was an important factor which plays key role in prevalence of diabetes mellitus. The Bhasma of gold is an important component present in the Vasant Kusumakar Ras which possess significant antioxidant activity^[11] and the Bhasma of Iron reduced the oxidative stress through DPPH free radical scavenging.^[12] Other Loha Bhasma are used in treatment of Prameha (Diabetes) which may contribute for restoration of blood glucose levels with Vasant Kusumakar Ras.^[9]

The Bhasmas are processed with herb decoctions of Vasa, Sandal wood, Vetiver, Turmeric, Banana, Lotus Jasmine flower and kasturi. These Bhavana Dravyas in the Vasant Kusumakar Ras formulation have their individual Pharmacological effects through different pathways involved in Pathogenesis of diabetes and related disorders.^[10]

The Important herbal principles of Vasant Kusumakar Ras include Vasa (*Adathoda Vasaka*) possesses anti-cataract and antioxidant activities through aldose reductase inhibitory activity.^[13] Petroleum ether extract of Sandal wood (*Santalum album*) produced the significant hypolipidemic activity which helps in preventing the insulin

resistance.^[14] Ethanol extract of Ushira (*Vetiveria Zizanioides*) significantly reduced the blood glucose levels of alloxan induced diabetes rats.^[15] Rheebera (*Pavonia Odorata*) root extract consists of several bioactive antidiabetic principles.^[16] Haridra (*Curcuma Longa*) consists of an important active constituent curcumin, well known therapeutic agent for treatment of complications of diabetes.^[17] Kadali (*Musa Paradisiaca*) consists of coumaric acid and caffeic acid, flavonol and anthocyanins Which had significant effects on the blood glucose levels of diabetic rats.^[18]

It has proposed that the effect of Vasant Kusumakar Ras attributed to activity profile of individual components (Bhasmas and Herbs) in the formulation which may be additive to produce the desired effect of Vasant Kusumakar Ras for the management of diabetes and its complications.^[10]

The current study focused on evaluating the effect of Vasant Kusumakar Ras on the normoglycemic animals as well as hyperglycemia animals during OGTT. The study was carried out by administering the test drug (25 mg/kg) for a period of seven days. Subsequently, OGTT test was performed in the same animals on 8th day. The blood glucose levels were significantly decreased post 7 days of drug treatment. Similarly, during the OGTT also the Vasant Kusumakar Ras significantly reduced the blood glucose levels. These studies indicated that Vasant Kusumakar Ras possess significant blood glucose lowering potential in normoglycemic as well as glucose induced hyperglycaemic SD rats (Fig.01 & Fig.02).

CONCLUSIONS

Our study establishes the significant hypoglycemic and antihyperglycemic effect of Vasant Kusumakar Ras in normoglycemic and hyperglycaemic animals. The results of the current study suggest the ethnopharmacological use of Vasant Kusumakar Ras to reduce the hyperglycemic episodes in diabetic and nondiabetic hyperglycemic subjects. Further investigations are in progress to establish the glucose lowering potential of Vasant Kusumakar Ras.

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Abbreviations:

ANOVA: Analysis of Variance, Hr: Hour, OGTT: Oral Glucose tolerance test, RH: Relative humidity, SD: *Sprague Dawley*; SEM: Standard error of mean, VEGF: Vascular endothelial growth factor, VK Ras: Vasant Kusumakar Ras

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