

# Role of Kataka-Khadiradi Ghanavati Ayurvedic Formulation in the Management of Diabetic Retinopathy

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## ABSTRACT

**Introduction:** Metabolic disorders are considerable health issues due to their association with morbidities and mortalities. Diabetes is one of the metabolic disorders associated with every systemic morbidity. Diabetic retinopathy (DR) is one of such morbidity which is vision-threatening and the whole world is looking for a solution. In contemporary science, there are management techniques which are applicable when DR is completely manifested. **Objectives:** The objective of this study was to review existing pharmaco-analytical reports on Katakakhadiradi Kashaya (KKK) and Ghanavati and its contents, animal studies and clinical trials of management of diabetes, and its complications through the KKK and Ghanavati (KKG). **Design:** The literature research comprised an electronic database from January 2000 to February 4, 2023. The study included MEDLINE, PubMed, the Cochrane Library, Google Scholar, AYUSH Research Portal, and DHARA database. Search terms were used "KKK", "DR", "Katakakhadiradi Ghanavati", and "Antioxidants." No limits were used. The search strategy was adapted for each database as necessary. Pharmaco-analytical reports and animal studies were included in the current review. The study applied inclusion criteria while screening the records. **Intervention:** Phytochemical constituents and their effect on DR. **Outcome measures:** Number and results of studies identified in the review. **Results:** The integrative approach could open new hope for patients of DR and is a need of time.

**Keywords:** Katakakhadiradi Ghanavati, Diabetic Retinopathy, Oxidative stress

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## INTRODUCTION

Diabetes is now a global concern, with drastic rise of incidence all over the world.<sup>[1]</sup> The global prevalence of diabetes mellitus is predicted to increase dramatically in the coming decades, from an estimated 382 million in 2013–592 million by 2035 (Duh EJ, Sun JK, Stitt AW. "Diabetic retinopathy (DR): Current understanding, mechanisms, and treatment strategies." JCI insight vol. 2, 14 e93751. 20 Jul. 2017, Doi: 10.1172/jci.insight.93751). Macrovascular and microvascular complications of diabetes will lead to morbidity and pre-mature deaths. DR is one of the microvascular morbidities caused by pathology of the capillaries, arterioles, and venules in the retina and is the leading cause of visual impairment and irreversible blindness in advanced conditions.<sup>[2-4]</sup> According to the World Health Organization, DR accounts for 4.8% of the 37 million cases of blindness worldwide in the year 2002<sup>[5]</sup> and is going to high by 2045 as per the American Association of Ophthalmology. Multicentric study to estimate prevalence says that, in absolute numbers, approximately 3 million people aged 40 years or older have vision-threatening DR in India, with a higher prevalence in those with known diabetes residing in high and middle ETI–SDI states.<sup>[6,7]</sup> The incidence of DR is much more high in type II diabetes in comparison with type I.<sup>[8-10]</sup>

Herbal formulations have emerging with a major role in metabolic diseases such as diabetes, hypertension, and hyperlipidemia which are associated with severe life-threatening morbidity and mortality.<sup>[11]</sup> Katakakhadiradi ghanavati is the tablet formulation developed from the Katakakhadiradi Kashaya (KKK). KKG is polyherbal tablet formulation of Kashaya of total 12 herbal components: Kataka (*Strychnos potatorum*), Khadira (*Acacia catechu*), Amalaki (*Embelica officinalis*), Daru haridra (*Berberis aristata*), Samanga (*Biophytum sensitivum*), Vidula (*Barringtonia actinangula*), and Abda (*Cyperus rotundus* (Cyclea peltata)). KKK is known for its anti-inflammatory and anti-microbial activity. It helps to heal wounds and ulcers as well as skin conditions including

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acne. The antioxidant, anti-inflammatory, and hepatoprotective qualities of KKK may be responsible for its antidiabetic effect.<sup>[12-14]</sup>

In the current review, limitless search words "Katakakhadiradi Ghanavati," "Oxidative stress," and "DR," to search PubMed, Scopus, and Google Scholar completely up to January 2022. In addition, diligently browsed Google Scholar and the citations of important articles. Furthermore, looked through abstracts of unavailable articles, and then the report was acquired.

## DR and its Management

DR is progressive complication associated with diabetes. As DR is the manifestation of both vascular and non-vascular tissue pathology, but microvascular components are of major features. Changes in microvascular tissue are used as standard parameters of assessment. Earlier stage of DR is non-proliferative DR (NPDR) and the advanced stage as PDR. Further, NPDR is based on pathological microvascular features such as microaneurysms, retinal hemorrhages, intraretinal exudates, leaks or blockage abnormalities, and venous caliber changes, meanwhile, PDR is specifically characterized by abnormal pre-retinal neovascularization. Another progressive abnormality in DR due

to derangement of the blood–retinal barrier and neural retina is known as diabetic maculopathy. Irrespective of the stage of progression, DR changes will contribute to the various degree of vision impairment and lands up in blindness ultimately.<sup>[15]</sup>

DR and its vision-threatening quality made special emphasis on the prevention and early detection as important tools in action to reduce DR. As DR is due to vascular tissue pathology due to hyperglycemia, early prevention can be done with glycemic and lipid controls. Well-controlled hypertension in diabetes patients was shown the less progression of the DR and related complications.<sup>[16]</sup> However, primary preventive measures are beneficial to delay the progress of DR, but well-established DR is necessarily to be managed to preserve sight and can be done with laser photocoagulation, intravitreal injections of steroids, and anti-VEGFs, vitrectomy, etc. modes of management as the needs of the patients.<sup>[17]</sup> The abovementioned management techniques are effective at preserving sight and also result in improvement in vision for patients with advanced DR. However, some of the limitations such as interventional procedures and economical burden are still exist. Hence, non-invasive, prolonged therapies are required for the management of DR.<sup>[3]</sup>

### Khatakhadiradi Ghana Vati as Antidiabetic Formulation

Kataka khadiradi ghanavati is a herbal formulation made up Kashaya of 12 herbal drugs. Polyherbal formulation is having more efficacy than single herbal formulation. This polyherbal formulation is known for its anti-diabetic activity. As it is already established that proper hyperglycemic control and well-managed lipid profile are key factors to prevent DR. In that case, the contents of Kataka Khadiradi Ghanavati are well known for their specific antidiabetic effects with their anti-inflammatory and antioxidant activity.<sup>[14]</sup> The current review work is suggestive that drugs used in the formulation are well-proven for their antioxidants, anti-inflammatory, hypoglycemic, and hepatoprotective activities. These are beneficial for the maintenance of normal blood glucose levels, warn off the inflammatory reactions of free radicals, and maintain the health of the retina.<sup>[15]</sup>

### DISCUSSION

The obscured metabolic pathway causing DR, especially of non-proliferative type, is not well understood. However, probable postulations are reviewed as follows:

1. Formation of microaneurysms as a result of retinal pericytes death due to electrolyte imbalance induced by high aldose reductase.<sup>[18]</sup>
2. Accumulation of the extracellular fluids due to abnormal retinal hemodynamic as a result of leukostasis, non-perfusion, and endothelial lining damage.<sup>[19]</sup>

The abovementioned factors are the responsible introduction of VEGFs leading to neovascularization in retina i.e. advanced DR.

Kataka herb seeds are having alkaloids, tannins, and flavonoids, and are proven with antidiabetic activity in alloxan-treated diabetic animal models by reducing the blood glucose level, initial lipid level, and increases insulin levels.<sup>[20]</sup> Naturally occurring bio-active compounds in Khadira such as catechin and epicatechin known for functions as an anti-angiogenic activity, mitochondrial adhesion inhibition, and protein kinase inhibition activity which play a key role in resolving the pathology of DR; similarly, tannins

are found to be responsible for astringent action of healing. This bioactivity of the khadira are may helpful in resolving the hypoxic tissue insult-induced VEGFs.<sup>[21]</sup> Amalaki phytoconstituents, such as vitamin C, polyphenols, flavonoids, and tannins, have potential benefits in DR by reducing oxidative stress. Even studies suggestive that amalaka reduces blood sugar type II diabetes.<sup>[22-25]</sup> The other constituent Katakakhadiradi ghanavati also helpful in reducing oxidative stress and by maintaining the health of retina.<sup>[26]</sup> KKK is classical Kashaya formulation, and ghanavati is concentrated form that gives an add-on effect.

### CONCLUSION

DR is the complication of diabetes which is mainly due to uncontrolled high blood glucose sugar levels and associated morbid conditions such as hypertension and increased lipid profile. The management of the DR is of utmost need as it is a major cause of preventable blindness. Prevention of the DR is not possible in all patients. There are many therapies to treat well-established DR and its complications but every management has their own limitations hence there is a need of alternative therapy for the management of DR which is not non-invasive and easily adaptable can be used for prolonged use Kataka Khadiradi Kashaya Ghanavati and its contents are known for its anti-diabetic activity and can be a wonderful remedy in case of management of DR.

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