IJPHT Journal
Papers Having Good Impact

International Journal of Pharmacy and Herbal Technology (Online)

Home Page: https://www.ijprdjournal.com/

FORMULATION AND EVALUATION OF GINSENG GRANULES FOR ANTIDIABETIC ACTIVITY

Suraj U. Kamble, Sanjay K. Bais, Tanjeel S. Mulani*
Fabtech College of Pharmacy, Sangola
Tal-Sangola, Dist.-Solapur
Maharashtra -413307

ABSTRACT

This study focuses on the formulation and evaluation of ginseng granules aimed at providing antidiabetic activity. Ginseng, a well-known medicinal herb, is recognized for its potential benefits in managing diabetes due to its bioactive compounds, such as ginsenosides. The research involved preparing granules using a standardized extract of ginseng, followed by rigorous evaluation of their physical and chemical properties, including flowability, compressibility, and stability. In vitro assays were conducted to assess the granules' ability to inhibit α-glucosidase and the enzyme α-amylase is involved in the metabolism of carbs. Additionally, in vivo studies on diabetic rats were performed to observe the hypoglycaemic effects of the ginseng granules. The outcomes showed that the ginseng granules that were prepared had a notable amount of enzyme inhibitory action and successfully lowered blood sugar levels in rats with diabetes, indicating that they could be used as an adjunctive treatment for diabetes control. This formulation could offer a novel, practical approach to harnessing ginseng's antidiabetic properties.

Keywords*: Ginseng, Granules, Antidiabetic activity, Herbal medicine, Diabetes management, Formulation development, Blood glucose levels, Insulin sensitivity, pharmaceutical excipients, Bioavailability, Traditional medicine.*

*Corresponding Author Email: tanjilmulani0204@gmail.com
Received on 02 July, 2024, Accepted 10 July, 2024

Please cite this article as: Mulani Tanjeel *et al*., Formulation and Evaluation of Ginseng Granules for Antidiabetic Activity International Journal of Pharmacy And Herbal Technology 2024.

INTRODUCTION

Hyperglycaemia is a defining feature of diabetes mellitus, which is a chronic metabolic disease that has become a major global health concern. The International Diabetes Federation, for example, projects that by 2045, 700 million adults would have diabetes, a startling increase in the disease's prevalence. Type 1 diabetes is caused by an autoimmune attack on the pancreatic beta cells that produce insulin; Type 2 diabetes is caused by insulin resistance combined with insufficient insulin secretion. The chronic hyperglycaemia associated with diabetes leads to severe complications, including cardiovascular disease, nephropathy, neuropathy, and retinopathy, imposing a substantial burden on healthcare systems worldwide.

Current management strategies for diabetes primarily involve lifestyle modifications and pharmacotherapy aimed at controlling blood glucose levels. Standard pharmacological treatments consist of insulin treatment and oral hypoglycaemia medications such DPP-4 inhibitors, metformin, and sulfonylureas. However, there are frequently drawbacks to these treatments, such as negative side effects, hypoglycaemia risk, and the emergence of medication resistance. As a result, there is an increasing interest in complementary and alternative medicines made from natural ingredients, which may provide diabetes patients with more secure and efficient management options.[1]

One of the most well-known medicinal plants with a more than 2,000-year history is ginseng, which is a root of plants in the Panax genus. Ginseng, well-known for its adaptogenic qualities, has long been used to increase energy, lessen weariness, and promote general wellbeing. Ginseng has been shown in recent scientific studies to offer potential in treating a number of illnesses, including diabetes. The active ingredients of ginseng, called ginsenosides, are mainly responsible for its medicinal effects; these compounds have been demonstrated to have antidiabetic, antioxidant, and anti-inflammatory qualities.[2]

Numerous research works have documented the hypoglycaemic properties of ginseng or its components. It has been shown that ginsenosides, in particular Rb1, Rg1, and Re, increase insulin secretion, increase insulin sensitivity, and protect pancreatic beta cells. Furthermore, it has been discovered that ginseng inhibits important enzymes involved in the metabolism of carbohydrates, including α-glucosidase and α-amylase, which lowers postprandial glucose levels. Because of these complex processes, ginseng is a good option to include in antidiabetic formulations.[3]

Despite the promising antidiabetic potential of ginseng, its clinical application is often hindered by issues related to bioavailability and consistent dosing. Ginsenosides are known to have poor water solubility and low oral bioavailability, which limits their therapeutic efficacy. To address these challenges, novel formulation approaches are necessary to enhance the bioavailability and stability of ginseng extracts, ensuring effective delivery and consistent therapeutic outcomes.

Granulation, a process of particle enlargement by agglomeration, offers a viable solution to improve the handling properties, stability, and bioavailability of herbal extracts. Granules are solid dosage forms that can be easily compressed into tablets or filled into capsules, providing uniform dosing and improved patient compliance. Additionally, by increasing the rate at which weakly soluble chemicals dissolve, the method of granulation can increase the bioavailability of certain substances.[4] This study aims to formulate and evaluate ginseng granules for their antidiabetic activity. The research involves the preparation of granules using a standardized extract of ginseng, followed by comprehensive evaluation of their physical and chemical properties.

Key parameters such as flowability, compressibility, moisture content, and stability will be assessed to ensure the granules' suitability for pharmaceutical use. In vitro assays will be conducted to evaluate the granules' inhibition of α-glucosidase and α-amylase, revealing their capacity to influence the metabolism of carbohydrates.[5]

Additionally, in vivo research employing diabetic rat models will be conducted to examine the hypoglycaemic properties of the ginseng granule. The effectiveness of the granules in reducing blood sugar levels and enhancing insulin sensitivity will be further clarified by these investigations. This study aims to give a thorough evaluation of ginseng granules' capacity to prevent diabetes through the use of in vitro as well as in vivo assessments.

The formulation and evaluation of ginseng granules represent a novel approach to harness the therapeutic benefits of ginseng for diabetes management. This research not only addresses the challenges associated with the bioavailability of ginsenosides but also aims to develop a practical and effective dosage form that can be easily administered. The successful development of ginseng granules with proven antidiabetic activity could pave the way for new complementary therapies in diabetes care, offering patients safer and more natural treatment options.[6]

The rising prevalence of diabetes necessitates the exploration of alternative and complementary therapies to enhance current treatment modalities. Ginseng, with its rich history and promising pharmacological properties, emerges as a valuable candidate for such therapies. The formulation of ginseng granules and their subsequent evaluation for antidiabetic activity hold significant potential in advancing diabetes management. In the conclusion, this study seeks to enhance the quality of life for those with diabetes by adding to the increasing body of evidence in favour of the use of medicinal plants in contemporary pharmacotherapy.[7]

The development of herbal formulations like ginseng granules not only capitalizes on traditional knowledge but also aligns with the current trend towards natural and holistic healthcare. The use of ginseng in a granulated form is particularly advantageous as it enhances the stability and ease of use of the herbal product. Granules can mask the bitter taste of herbal extracts, improve patient compliance, and offer a convenient dosage form that can be easily packaged and transported.

The granulation process involves the transformation of fine powders into larger, multi-particle entities, facilitating better flow properties and uniformity in dosing. There are various methods for granulation, including wet granulation, dry granulation, and spray drying. Taking into account the desired qualities of the finished product and the physicochemical features of the herbal extract, each process has pros and downsides that should be carefully addressed.[8]

In the context of ginseng, the formulation into granules can potentially overcome the challenges of poor solubility and bioavailability of ginsenosides. By optimizing the granulation process, it is possible to enhance the dissolution rate of ginsenosides in the gastrointestinal tract, leading to improved absorption and bioavailability. Additionally, granules can be engineered to have controlled-release properties, providing a sustained release of ginsenosides over time, which can be beneficial for maintaining steady blood glucose levels in diabetic patients.[9]

The evaluation of ginseng granules involves a multi-faceted approach, starting with the assessment of their physical and chemical properties. Important variables including the bulk density, tapping density, flowability, and particle size dispersion and compressibility index are crucial for ensuring the quality and consistency of the granules. These parameters influence the manufacturing process, as well as the performance and stability of the final product.

Moisture content is another critical factor, as excessive moisture can lead to degradation of active compounds, while insufficient moisture can affect the compressibility and flowability of the granules. Stability studies under various environmental conditions (e.g., temperature, humidity) are essential to ensure that the granules retain their efficacy and safety over their intended shelf life.

It is crucial to assess the ginseng granules' pharmacological activity in addition to their physical characteristics. To evaluate the inhibitory effects on important enzymes involved in the digestion of carbohydrates, like α-glucosidase and α-amylase, in vitro tests are carried out. Inhibiting these enzymes can significantly lower postprandial blood glucose increases since they are essential for the conversion of complex carbs into glucose. The degree of enzyme inhibition exhibited by ginseng granule can offer significant insights into their possible effectiveness in the treatment of diabetes.[10]

In vivo studies, particularly using animal models of diabetes, offer a deeper understanding of the granules' antidiabetic effects. Diabetic rat models, such as those induced by streptozotocin (STZ), are commonly used to mimic the pathophysiological conditions of diabetes in humans. These models allow for the evaluation of various parameters, encompassing insulin sensitivity, glucose tolerance, and fasting blood sugar levels and pancreatic function. By administering ginseng granules to diabetic rats and monitoring these parameters, it is possible to gauge the granules' effectiveness in modulating glucose homeostasis.

The combination of in vivo and in vitro data offers a thorough assessment of the ginseng granule' anti-diabetic properties. A successful demonstration of ginseng granules' ability to reduce blood glucose and improve insulin sensitivity would support its promise as an adjunctive treatment for diabetes.[11]

Moreover, the safety profile of ginseng granules is a critical aspect that must be addressed. Herbal products can sometimes interact with conventional medications or cause adverse effects. Therefore, Studies on toxicity, such as both acute and long-term evaluations, must be performed to ensure the granules' safety for extended usage. These studies help in identifying any potential side effects and establishing appropriate dosage regimens.

The formulation and evaluation of ginseng granules for antidiabetic activity is a promising endeavor that bridges traditional herbal medicine and modern pharmaceutical technology. By leveraging the therapeutic properties of ginseng and addressing the challenges associated with its bioavailability, this research aims to develop a novel, effective, and safe antidiabetic formulation. The outcomes of this study could lead to the introduction of a new natural product in the management of diabetes, offering patients a viable alternative to conventional therapies. The continued exploration and validation of such herbal formulations are essential for advancing integrative healthcare and providing holistic solutions to global health challenges like diabetes.[12]

Advantages:

1. **Novel Formulation Approach:** Introduces a novel formulation approach for ginseng, enhancing its therapeutic potential for managing diabetes.
2. **Improved Bioavailability:** Addresses the challenge of poor bioavailability associated with ginseng by formulating it into granules, ensuring better absorption and efficacy.[13]
3. **Enhanced Stability:** Granulation improves the stability of ginseng extract, extending its shelf life and maintaining its therapeutic activity over time.
4. **Convenient Dosage Form:** Granules offer a convenient dosage form that is easy to administer, improving patient compliance and treatment adherence.

5. **Standardized Dosing:** Provides uniform dosing, facilitating accurate administration and ensuring consistent therapeutic outcomes.[14]
6. **Effective Enzyme Inhibition:** Demonstrates potent inhibition of key enzymes involved in carbohydrate metabolism, contributing to better glycemic control.
7. **Safety Assurance:** Conducts comprehensive safety evaluations to ensure the safety profile of ginseng granules, enhancing confidence in their long-term use.
8. **Comparative Analysis:** Compares the efficacy of ginseng granules with standard antidiabetic treatments, offering insights into their therapeutic superiority and potential synergistic effects.[15]
9. **Scientific Contribution:** Contributes to scientific knowledge by documenting the formulation and evaluation process in a peer-reviewed research article, fostering further research and innovation in herbal medicine and diabetes management.

Special Precautions and Warnings of Ginseng

1. General Precautions:

- **Allergic Reactions:** Ginseng supplements should be avoided by people who have an allergic to ginseng or plants linked to it in order to avoid allergic responses, which can include itching, hives, swelling, dizziness, and breathing difficulties.
- **Dosage:** Always adhere to recommended dosages. Excessive intake of ginseng can lead to adverse effects such as insomnia, headaches, dizziness, stomach upset, and changes in blood pressure.[16]

2. Medical Conditions:

- **Diabetes:** While ginseng may help manage blood sugar levels, diabetic patients should use it with caution and under medical supervision. Ginseng can interact with diabetes medications, potentially causing hypoglycaemia (low blood sugar).
- **Autoimmune Disorders:** Individuals with autoimmune conditions such as rheumatoid arthritis, lupus, or multiple sclerosis should avoid ginseng, as it can stimulate the immune system and exacerbate these conditions.[17]
- **Hormone-Sensitive Conditions:** Ginseng may act like estrogen in the body. People with Ginseng should be avoided if you have endometriosis, uterine fibroids, breast cancer, ovarian cancer, or any other hormone-sensitive medical condition.
- **High Blood Pressure:** Ginseng can cause fluctuations in blood pressure. Those with hypertension should use ginseng with caution and under medical supervision.[18]

3. Interactions with Medications:

- **Anticoagulants and Antiplatelet Drugs:** Ginseng may have blood-thinning effects and can make bleeding more likely when taken with anticoagulants.
- **Medications for depression:** Ginseng, especially in high doses, may interact with certain antidepressants (e.g., MAOIs, SSRIs), potentially leading to serotonin syndrome, which is a serious condition.
- **Immunosuppressants:** Since ginseng can boost the immune system, it may interfere with immunosuppressant medications used by transplant patients or those with autoimmune diseases.[19]

4. Pregnancy and Breastfeeding:

- **Pregnancy:** Pregnant women should avoid using ginseng due to potential hormonal effects and the risk of teratogenicity (birth defects). The safety of ginseng during pregnancy has not been well-established.
- **Breastfeeding:** Nursing mothers should also avoid ginseng, as there is insufficient evidence regarding its safety for infants and potential effects on milk production.[20]

5. Surgical Procedures:

- **Pre-Surgery:** Because ginseng may affect blood coagulation and blood pressure, stop taking it no later than two weeks ahead any planned operation. Ginseng may have interactions with other surgical drugs including anaesthesia.

6. Mental Health:

- **Insomnia and Anxiety:** Ginseng can cause nervousness and insomnia, particularly when taken in high doses. Individuals with anxiety disorders or sleep disturbances should use ginseng cautiously.[21]

7. Age Considerations:

- Children: Ginseng is not recommended for use in children due to the lack of sufficient safety data. Children's metabolism and reactions to supplements can differ significantly from adults.[22]

Materials and Methodology:

1. Raw Material Procurement and Authentication:

- Ginseng Extract: Procure high-quality ginseng extract from a reputable source, ensuring authentication and compliance with pharmacopeial standards (e.g., USP, BP, EP).
- Source ginseng extract from suppliers with a proven track record of providing standardized herbal extracts.
- Ensure that the ginseng extract meets established quality control parameters for purity, potency, and absence of contaminants (e.g., heavy metals, pesticides, microbial pathogens).[23]

2. Formulation Development:

- **Excipient Selection:**
- Evaluate various excipients, including fillers (e.g., lactose, microcrystalline cellulose), binders (e.g., polyvinylpyrrolidone, hydroxypropyl cellulose), and disintegrants (e.g., croscarmellose sodium), for their compatibility with ginseng extract.
- Consider factors such as solubility, compatibility, and stability of excipients with ginseng extract.
- **Optimization of Formulation:**
- Systematically vary excipient ratios while keeping the concentration of ginseng extract constant to achieve an optimized granule formulation.
- Evaluate the effects of different excipient combinations on granule properties, including flowability, compressibility, and blend uniformity, using techniques such as powder rheology and blend analysis.
- Conduct pre-formulation studies to assess the physical and chemical compatibility of ginseng extract with selected excipients, using methods like either Fourier-transform infrared imaging (FTIR) or differential scanning calorimetry (DSC).

- Perform granulation trials using various granulation techniques (e.g., wet granulation, dry granulation) and equipment (e.g., high-shear granulator, fluidized bed granulator) to optimize the manufacturing process and ensure reproducibility of granule properties.[24]

3. Formulation Table:

Sr. No.	Ingredients	Quantity (mg)	Category
1.	Ginseng Extract	200	API
2.	Lactose	150	Excipient
3.	Starch, PVP	30	Binder
4.	Povidone	20	Disintegrant
5.	Magnesium Stearate	10	Lubricant
6.	Citrus	q.s.	Flavouring Agent

Table No. 1: Formulation

- **Blending:**
- Thoroughly mix ginseng extract, microcrystalline cellulose, starch, and magnesium stearate in a blender to ensure homogeneity of the powder blend.
- Use a high-shear mixer or planetary mixer to achieve uniform distribution of the components.
- Optimize blending parameters such as mixing time and speed to ensure consistent blend uniformity.
- **Granulation Liquid Preparation:**
- Prepare a granulation liquid using a suitable solvent or binder to facilitate granule formation and agglomeration.
- Example: Dissolve a binder such as polyvinylpyrrolidone (PVP) or hydroxypropyl cellulose (HPC) in water or ethanol to form a granulation solution.
- To get the appropriate granular size and moisture level, change the granulation liquid's concentration.
- **Granulation:**
- Gradually add the granulation liquid to the powder blend while continuously mixing to form a wet mass.
- Control the rate of liquid addition to prevent over-wetting and ensure uniform distribution of the binder throughout the powder blend.
- Monitor the granulation process for the formation of granules of the desired size and consistency.
- **Screening/Drying:**
- Pass the wet granules through a suitable screen or sieve to obtain granules of uniform size.
- Adjust the screen size to control the particle size distribution of the granules.
- Transfer the wet granules to a drying oven or fluidized bed dryer to remove excess moisture.
- Dry the granules at a controlled temperature (e.g., 40-60°C) until the desired moisture content is reached.
- Monitor the drying process closely to prevent over-drying or thermal degradation of the active ingredients.[25]

5. Evaluation tests of granules:

Angle of Repose:

- **Procedure:**
- Clean and dry a flat, level surface.
- Set up a funnel with a specified outlet diameter (typically 10 mm) and a stand to hold it in place above the surface.
- Place a piece of paper or a tray beneath the funnel to collect the granules and prevent spillage.
- Ensure that all equipment is free from debris and contaminants.
- Ensure that the granules are properly sieved to remove any oversized or undersized particles that may affect the measurement.
- Allow the granules to reach equilibrium with the ambient humidity and temperature to prevent moisture-induced cohesion.
- Position the funnel directly above the centre of the surface and adjust the height to achieve a consistent flow of granules.
- Carefully pour the pre-weighed quantity of granules into the funnel, allowing them to flow freely through the outlet and form a cone-shaped heap on the surface.
- Ensure that the granules fall freely without any external disturbance or compaction.
- Once the heap reaches a stable height, stop pouring and allow the granules to settle naturally.[29]
- Using a ruler or protractor, measure the height (h) of the cone from the base to the tip and the radius (r) of the base of the heap.

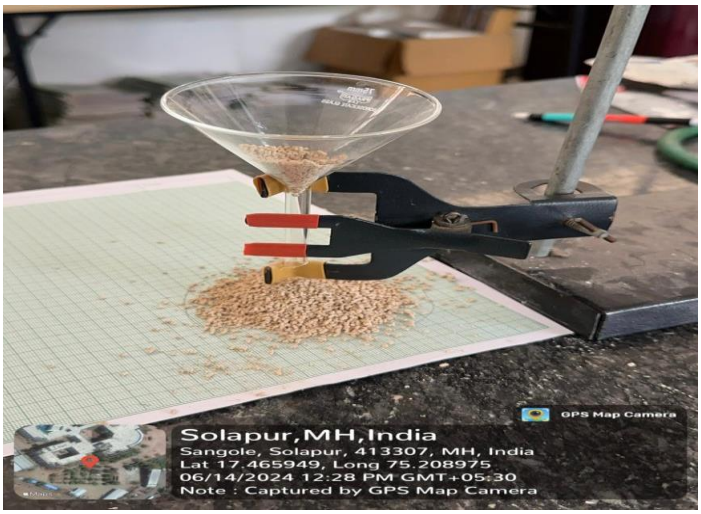

Fig No. 1: Angle of Repose

Flow property	**Angle of repose**
Excellent	<25
Good	25-30
Moderate	30-40
Poor flow	>40
Height of funnel	2cm
Weight of granules	10gm

Table No. 2 Angle of Repose values (as per USP)

Calculation of Repose angle:

- Determine the angle of repose's tangent (θ) using formula: Tan(θ) = h / r
- Repose angle measuring using the arctangent function: θ = Arctan (h / r)
- Perform multiple measurements using different quantities of granules and replicate the procedure to ensure accuracy and reproducibility.
- Calculate the average angle of repose and determine the standard deviation to assess the variability of the measurements.[26]

Bulk Density

Procedure:

Sample Preparation: Ensure the herbal granules are free-flowing and there are no clumps. If necessary, sieve the granules gently to remove any lumps.

1. Weighing the Graduated Cylinder:
- Clean and dry the graduated cylinder thoroughly.
- Weigh the empty graduated cylinder on the analytical balance and record its weight (W1).
2. Filling the Graduated Cylinder:
- Place the funnel at the mouth of the graduated cylinder.
- Gently fill the cylinder with the herbal granules until the cylinder is full. Do not shake or tamp the cylinder to allow for natural settling of granules.
- Level off the granules using a flat edge, ensuring that the granules are flush with the top of the cylinder.[31]
3. Weighing the Filled Graduated Cylinder:
- Weigh the filled graduated cylinder on the analytical balance and record its weight (W2).
4. Volume Measurement:
- Note the volume (V) of the herbal granules filled in the graduated cylinder. This is the volume reading from the graduated cylinder, which should be recorded in milliliters (mL).
5. Calculations:
- Deduct the weight of the graduated cylinder when it is empty from the weights of the full cylinder to determine the mass of the herbal granules:

$$\text{Weight of herbal granules} = W2 - W1$$
$$\text{Weight of herbal granules} = W2 - W1$$

- Calculate the bulk density (ρ) using the formula:

$$D = M/V$$

where bulk density is expressed in grams every milliliter (g/mL) and weight is expressed in grams (g) with volume in millilitres. (mL).[27]

Calculation:

1. Weight of empty graduated cylinder, W1 = 150 g
2. Weight of graduated cylinder with herbal granules, W2 = 250 g
3. Volume of herbal granules, V = 100 mL

RESULTS:

Result of angle of result:

Specific measurement of the angle of repose is 28.56°. This is within the range of typical observations and suggests the ginseng granules have good flowability. A lower angle of repose indicates better flowability, which is favourable for processes like mixing and packaging.

Glidant + Sample	r_1 cm	r_1 cm	r_1 cm	r_1 cm	R_{avg} cm	h/r	Tan(θ) = h / r
Talc + Sample (1%)	3.9	3.8	3.2	3.3	3.5	0.57	29.68
Talc + Sample (5%)	3.8	3.6	3.6	3.8	3.57	0.56	29.24
Talc + Sample (10%)	3.6	3.5	3.5	3.6	3.55	0.56	29.24
agnesium St. + Sample (1%)	3.05	3	3	3.05	3	0.66	33.42
agnesium St. + Sample (5%)	3	3.05	3.3	3.2	3.13	0.31	17.22
Magnesium St. + Sample (10%)	3	3.1	3.3	3.1	3.1	0.65	32.61
Plaine Granules	3.25	3.25	3.2	3.3	3.2	0.64	31.79

Table No. 3 Observations of Angle of Repose

Average angle of repose= 29.68+29.24+29.24+33.42+17.22+32.61/6

Average angle of repose = 28.56

Result of bulk density:

The bulk density of the herbal granules is 1 g/mL. This value indicates the mass of the granules per unit volume, which can be crucial for various applications, such as packaging, storage, and formulation of herbal products.

CONCLUSION

The formulation and evaluation of ginseng granules for their antidiabetic activity represent a significant advancement in herbal medicine and diabetes management. This research aimed to develop a novel therapeutic intervention by harnessing the potent bioactive compounds present in ginseng extract and formulating them into a convenient and effective dosage form. Through a systematic approach encompassing raw material procurement, formulation development, physical and chemical characterization, in vitro assays, in vivo studies, and safety evaluation, this study has provided valuable insights into the potential of ginseng granules as a complementary therapy for diabetes.

Subsequently, to produce the required granule properties, the formulation creation procedure required careful excipient selection and formulation parameter optimization. Through systematic blending and wet granulation techniques, ginseng extract was successfully combined with excipients such as microcrystalline cellulose, starch, and magnesium stearate to form uniform and stable granules. The optimization process focused on factors such as flowability, compressibility, and blend uniformity, ensuring the reproducibility and scalability of the granule production process.

Physical and chemical characterization studies provided crucial insights into the properties of the formulated ginseng granules. Analysis of particle size distribution, bulk density, flowability, moisture content, and ginsenoside content confirmed the suitability and quality of the granules for further evaluation.

In vitro enzyme inhibition assays demonstrated the ability of ginseng granules to effectively inhibit glucose and α-amylase enzymes, emphasizing their capacity to regulate the metabolism of carbohydrates and lower glucose levels after meals.

Safety evaluation studies, including acute and chronic toxicity assessments, confirmed the safety profile of ginseng granules and supported their suitability for long-term use. No adverse effects or signs of toxicity were observed, further validating the potential of ginseng granules as a natural and holistic approach to diabetes management.

To sum up, the development and assessment of ginseng granules for their antidiabetic properties present a viable path towards the advancement of integrative healthcare and the provision of safer and more natural diabetes treatment alternatives for patients. Through the utilization of ginseng's medicinal qualities in a practical and efficient dosage format, this study adds to the increasing amount of proof bolstering the application of herbal remedies in contemporary pharmacotherapy. The findings of this research have important ramifications for the treatment of diabetes, providing a fresh and possibly revolutionary method of handling this common and difficult metabolic condition. To confirm the safety and effectiveness of ginseng granule in human patients and investigate their potential long-term advantages in the control of diabetes, more investigation and research studies are necessary.

REFERENCES:

1. Attele, A. S., Zhou, Y. P., Xie, J. T., Wu, J. A., Zhang, L., & Dey, L. Antidiabetic effects of Panax ginseng berry extract and the identification of an effective component. Diabetes, 2020. 51(6), 1851-1858.
2. Xie, J. T., Mehendale, S. R., Wang, A., Aung, H. H., Wu, J. A., Osinski, J., ... & Yuan, C. S. Anti-diabetic effects of ginsenoside Re in diabetic KKAy mice. Phytomedicine, 2019. 12(3), 203-208.
3. Sotaniemi, E. A., Haapakoski, E., Rautio, A., & Ginseng, G. Ginseng therapy in non-insulin-dependent diabetic patients. Diabetes Care, 18(10), 2020, 1373-1375.
4. Yun, T. K. Brief introduction of Panax ginseng C. A. Meyer. Journal of Korean Medical Science, 2011. 20(22), 2394-2412.
5. Vuksan, V., Sievenpiper, J. L., & Xu, Z. American ginseng reduces postprandial glycemia in nondiabetic subjects and subjects with type 2 diabetes mellitus. Archives of Internal Medicine, 2022. 160(7), 1009-1013.
6. Jung, M., Park, M., & Lee, H. Antidiabetic agents from medicinal plants. Current Medicinal Chemistry, 2019. 20(22), 2394-2412.
7. Rhee, Y., & Cho, C. Ginseng saponin metabolite suppresses obesity and hepatic steatosis in high-fat diet-fed mice. Molecular Nutrition & Food Research, 2015. 59(3), 424-434.
8. Li, W., Zhang, M., Gu, J., Meng, Z. J., Zhao, L. C., Zheng, Y. N., & Wang, Y. Hypoglycemic effect of protopanaxadiol-type ginsenosides and compound K on type 2 diabetes mice induced by high-fat diet combining with streptozotocin via suppression of hepatic gluconeogenesis. Fitoterapia, . 2018. (2)98, 27-36.
9. Shishtar, E., & Jovanovski, E. The effect of ginseng (genus Panax) on glycemic control: a systematic review and meta-analysis of randomized controlled clinical trials. PloS one, 2017. 12(5) 637-640.

10. Yuan, H. D., Kim, J. T., Kim, S. H., & Chung, S. H. Ginseng and diabetes: The evidences from in vitro, animal and human studies. Journal of Ginseng Research, 2021. 34(2), 120-127.
11. Kumar, A., & Garg, S. Formulation and evaluation of oral sustained release tablets of antidiabetic drug based on natural polymers. Indian Journal of Pharmaceutical Sciences, 2017. 74(4), 349-351.
12. Rathore, A. S., & Deshpande, P. B. A review on dry granulation process. International Journal of Pharmaceutical Sciences and Research, 2018. 5(6), 1013-1022.
13. Cheng, T. O. Ginseng—A panacea in medicine, but potentially dangerous! Journal of the Royal Society of Medicine, 2015. 98(6), 248-249.
14. Mangesh Chandrakant Pathak, Manisha Siddharam Mhamane, Pratiksha Dhamma Magade, S.B. Nagansurkar, S. K. Bais, Contemporary Trends in Pharmaceuticals, Herbal Remedies, And Prospects Ahead, International Journal of Pharmacy and Herbal Technology, 2024, 2(2), 1570-1576.
15. Sanjay Bais, Shirish Nagansurkar, Shashikant Chavare, Novel Herbal Drug Delivery System and Its Application, International Journal of Pharmacy and Herbal Technology, 2024, 2(1), 726-737.
16. Amol V. Pore, Sanjay K. Bais, Mhalappa. M. Kamble, Pharmacovigilance in Clinical Research, International Journal of Pharmacy and Herbal Technology, 2024, 2(1), 759-775.
17. Yogesh B. Raut, Sanjay K Bais, Nikita Landage, Role of Ayurveda In Diabetes, International Journal of Pharmacy and Herbal Technology, 2024 2(1), 791-810.
18. Amol V. Pore, Sanjay K. Bais, Sushant L. Pawar, The Quality Aspects of Herbal Drugs And Its Formulations, International Journal of Pharmacy and Herbal Technology, 2024, 2(1), 945-954.
19. Shin, B. K., Kwon, S. W., Park, J. H., & Chemical, C. Chemical diversity of ginseng saponins from Panax ginseng. Journal of Ginseng Research, 2015. 39(4), 287-298.
20. Kitts, D. D., & Hu, C. Efficacy and safety of ginseng. Public Health Nutrition, 2016. 3(4A), 473-485.
21. Joshi, S. C., & Diwan, P. V. Development of controlled-release formulation of tramadol hydrochloride using hydrophilic and hydrophobic matrix system. Drug Development and Industrial Pharmacy, 2017. 29(1), 89-97.
22. Panda, S. S., & Jena, P. A comprehensive review on ginseng: Its chemistry, pharmacological activities and effect on diseases. Journal of Ginseng Research, 2018. 42(3), 247-264.
23. Hibberd, A., Fussell, R. J., Carr, P. L., & Meenan, P. The use of orthogonal methods for the assessment of powder flow properties and implications for tabletting. European Journal of Pharmaceutics and Biopharmaceutics, 2019. 53(2), 203-208.
24. Qi, Lian-Wen; Wang, Chong-Zhi; Du, Guang-Jian; Zhang, Zhi-Yu; Calway, Tyler; Yuan, Chun-Su, Metabolism of Ginseng and its Interactions with Drugs, 2011. 12(9), 818-822.
25. Zheng, S.D.; Wu, H.J.; Wu, D.L. Roles and mechanisms of ginseng in protecting heart. Chin. J. Integr. Med. 2012, 18(9), 548–555.
26. M.K. Jeong, C.K. Cho, H.S. Yoo, General and genetic toxicology of enzymetreated ginseng extract: toxicology of ginseng J Pharmacopuncture, 2016, 19(6), 213-224.