Effect of Corn Silk Extract on Resperidone Induced Obesity in Rats

[1]Mr. Piyush Jatinbos Kajale, [2]Dr. Darekar Shrikant

[1]S.Y.M. Pharm. (SEM 4), Guide, [2]Asso. Professor (M. Pharm, Ph.D.)
[1]Faculty Of Science and Techncology, [2]Ratandeep College of Pharmacy,
[1]Savitribai Phule Pune University, Pune, [2]Jamkhed Tal- Jamkhed, Dist. Ahmednagar

I. INTRODUCTION

Antipsychotics are recommended as the initial, evidence-based treatment for schizophrenia and other primary psychotic disorders. Some antipsychotics are also approved for conditions such as bipolar disorder, treatment-resistant depression, autism, and Tourette's disorder. They are commonly prescribed off-label for conditions like borderline personality disorder, obsessive-compulsive disorder, anorexia nervosa, insomnia, delirium, and various forms of dementia including Alzheimer's disease. However, the effectiveness of these medications can be limited by their side effects, which need to be carefully balanced against their varying therapeutic benefits across these conditions.[3] Consequently, discussions about these medications often focus more on their side effects rather than their therapeutic benefits. This emphasis is underscored by the recommendation of experts and guidelines to select antipsychotics based on their side effect profiles, which can vary greatly, rather than on differences in efficacy, which are generally seen as comparable. For conditions other than psychosis or for off-label uses where the evidence supporting antipsychotic benefits is less clear, the discussion around side effects becomes crucial. Here, the balance between potential benefits and risks significantly influences decisions regarding the use of these medications. [2,1Risperidonee is an atypical antipsychotic used mainly to treat schizophrenia and bipolar disorder. It is effective for both new-onset schizophrenia and long-term maintenance, and can be administered orally or via intramuscular injection. Common side effects of Risperidonee include weight gain, movement disorders, dizziness, fatigue, constipation, and dry mouth. Other notable side effects include orthostatic hypotension (low blood pressure upon standing), allergic reactions, neuroleptic malignant syndrome, high blood sugar, seizures, and tardive dyskinesia. In older adults with dementia, its use is associated with an increased risk of death. Additionally, use during the later stages of pregnancy may cause movement disorders in newborns.[4,5] Second-generation antipsychotics (SGAs) are associated with a reduced risk of extrapyramidal symptoms compared to first-generation antipsychotics. However, their use can lead to adverse effects such as weight gain, impaired glucose tolerance, hyperlipidemia, and

increased adiposity[6,7]. These metabolic changes are linked to higher morbidity due to their association with conditions like hypertension, type II diabetes, stroke, and cardiovascular disease. The side effects of SGAs can limit their use and negatively impact patient adherence [10]. Among SGAs, Risperidonee and clozapine are particularly notable for their significant effects on weight gain and metabolic disturbances. [12] Several medications cause unexpected changes in body weight in humans, which could potentially uncover new avenues for treating obesity and overweight by understanding their mechanisms. Furthermore, such investigations might facilitate the development of drugs with fewer side effects. Notable instances include the weight loss effects of the antiseizure medication topiramate and the weight gain associated with the atypical antipsychotics Risperidonee and clozapine. Obesity and related metabolic diseases are the most important medical problems worldwide. Obesity, especially associated with long-term use of atypical antipsychotics, is dangerous and affects millions of people worldwide. Risperidonee is an atypical antipsychotic drug widely used in the treatment of schizophrenia. However, Risperidonee is also one of the most obesogenic drugs. Clinical studies show that approximately 86% of patients treated with Risperidonee experience weight gain or obesity. Long-term use may cause dyslipidemia and diabetes. These metabolic effects, which include hyperglycaemia, decreased insulin sensitivity, obesity, and dyslipidemia, are risk factors for cardiovascular disease and increase mortality in patients with schizophrenia. Additionally, long-term Risperidonee treatment increases the risk of typeII diabetes in psychiatric patients. Although existing drugs can reduce the effects of antipsychotic drugs that disrupt metabolism, there is a need for drugs that can treat the adiposity caused by Risperidonee. [14,15] The precise mechanisms responsible for these metabolic effects induced by SGAs remain complex and multifaceted, involving both the central and peripheral nervous systems. Enhanced lipogenesis triggered by increased enzymatic activity is one probable peripheral mechanism for SGA- induced adverse metabolic effects such as hyperlipidemia.

Berberine, an isoquinoline alkaloid found in various herbs like Coptis chinensis and Goldenseal, is an OTC drug in China for treating microbial diarrhea. It is also available in the U.S. as a dietary supplement. Recent studies have highlighted a range of pharmacological effects linked to berberine, including antimicrobial, anti-inflammatory, anticancer, antiobesity, anti-diabetic, anti-hyperlipidemia, antidepressant, and potential schizophrenia treatment properties. Furthermore, studies have explored ginger rhizome extracts for their potential to mitigate weight gain and enhance energy expenditure in rodent models fed high- fat diets. Additionally, Zingiber officinale (ZO) has been recognized for its antidepressant effects.

Objectives

Investigate the effect of corn silk extract on weight gain in risperidone -treated rats. Assess the impact on blood glucose levels, lipid profiles, and leptin levels.

Examine histopathological changes in tissues like liver, fat, and muscle.

To determine the effect of corn silk on Risperidonee induced obesity in rats 2. To examine the

effect corn silk extract of daily food intake in Risperidonee treated rats. 3. To examine effect of corn silk extract on Risperidonee induced dyslipidemia in glucose intolerance Risperidonee treated rats. 4. To measure effect of corn silk extract on liver weight and histopathological changes in Risperidonee treated rats.

II. RISPERIDONE

Risperidonee, an atypical antipsychotic, was first approved by the FDA in September 1996 for treating schizophrenia. Its introduction provided psychiatrists with a new option that reduced the risk of movement-related side effects compared to older antipsychotics. [26] Meta- analyses have consistently shown Risperidonee's effectiveness and minimal movementrelated side effects compared to typical and some atypical antipsychotics in treating schizophrenia.[27] However, due to concerns about metabolic problems and weight gain, most guidelines position Risperidonee as a second-line treatment for schizophrenia, similar to clozapine. [28] Despite this, many experienced clinicians believe Risperidonee has significant efficacy advantages over other antipsychotics and continue to prescribe it for patients with schizophrenia. This review explores the role of oral Risperidonee in managing adults with schizophrenia, focusing on recent evidence supporting its efficacy since its initial approval.

Generally, atypical antipsychotic medications are effective as standalone treatments for bipolar disorder but not typically for unipolar depression. Specifically, drugs like aripiprazole, asenapine, Risperidonee, quetiapine, and risperidone have demonstrated effectiveness when used alone in treating bipolar disorder. These medications have also been found effective as monotherapies for generalized anxiety disorder. In the context of unipolar depression, atypical antipsychotics are often used in combination with antidepressants such as SSRIs or SNRIs. Aripiprazole, brexpiprazole, and risperidone have shown effectiveness when added to antidepressants, particularly in cases of treatmentresistant depression. Recent research has even explored the anxiolytic effects of brexpiprazole when combined with the SSRI resuscitator in an animal model of PTSD. Additionally, emerging experimental treatments targeting histamine, adenosine, and trace amine-associated receptors show potential as future antipsychotic and antidepressant agents, resembling the mechanisms of contemporary atypical antipsychotics. This review discusses how these medications, both current and investigational, operate at neural levels to effectively treat both psychotic and affective disorders

1.1.1. Risperidonee is extensively researched and widely used as an antipsychotic medication, valued for its effectiveness despite concerns about metabolic side effects. However, significant gaps in our understanding of Risperidonee's pharmacokinetics remain. These include issues such as the different formulations available, the potential benefits of therapeutic drug monitoring (TDM), altered pharmacokinetic properties in special patient populations or those with medical conditions, the use of high doses of Risperidonee, and its interactions with other drugs.[40] Mechanism of action

Risperidonee, a second-generation antipsychotic, primarily acts on dopamine and serotonin receptors in the brain. It blocks dopamine D2 receptors in the mesolimbic

pathway, which reduces positive symptoms such as hallucinations, delusions, and disorganized thinking and behavior in patients. Risperidonee also acts as an antagonist on serotonin 5HT2A receptors in the frontal cortex, helping to alleviate negative symptoms like lack of pleasure, flat emotions, reduced speech, lack of motivation, and poor attention.[30]

2.1.2 Pharmacodynamics

Risperidonee is an antagonist at numerous histamine H1, α1-adrenoceptors, muscarinic M15 receptors, and monoaminergic (5HT2A/2C, 5HT3, 5HT6, D1-4). Risperidonee also exhibits modest bindings to β-adrenoceptors, benzodiazepines, and GABAA. A common feature of all currently available antipsychotics, such as Risperidonee, is their blockage of the D2 receptor. Additionally, 5HT2A receptors are blocked by second-generation antipsychotics, which may work as a mediator to prevent the occurrence of extra-pyramidal adverse effects and may also raise dopamine levels in the brain. It is believed that its therapeutic benefits are mostly mediated by antagonistic interactions with these receptors. Antagonistic interactions at dopamine and other receptors Some of the negative effects of Risperidonee may be explained by 5HT2A.

CornSilkandItsPotentialBenefits Composition

2.7. Corn silk

Corn silk is a yellow silky component that grows on top of the corn cob (corn fruit) and is a part of the female flower (stigma) of the corn plant (Zea mays L.). Additionally, corn silk is a major by-product of the corn processing industry that is traditionally discarded as eco- friendly agricultural waste or used as animal feed. However, corn silk is a good source of vital nutrients, including carbohydrates, proteins, vitamins, and minerals, as well as resins, mucilage, and fibers. In addition, it also contains a wide range of bioactive compounds in the form of volatile oils, steroids, and other natural antioxidants, such as polyphenols and flavonoids. According to the traditional Chinese medicine system, these bioactive and fibrous compounds possess various health benefits and help to avoid numerous chronic diseases, including edema, cystitis, gout, rheumatism, and rheumatoid arthritis. In addition, several in vivo and clinical studies reported corn silk safe for human consumption. Given these benefits, corn silk is now being utilized in the development of value-added foods, such as beverages and patties. Furthermore, earlier studies of 10 different corn silk genotypes showed a significant number of bioactive components, including flavonoids and phenolics, and also revealed the antioxidant activities of corn silk polysaccharides; however, this characterization based on various techniques is not studied for corn silk powder. As corn silk nutrients and bioactives are mostly subject to large variations owing to soil conditions, environmental variations, and different cultivars, the current study aims to investigate the nutritional composition, bioactive composition.

2.7.2. Phytochemical composition

Phytochemicals are the non-nutritional bioactive compounds found in various parts of plants. In plants these compounds perform vital functions particularly protection from predators and harsh environmental conditions. These compounds are also important in pharmaceutical and medicinal field due to their antioxidant, antimicrobial, and other biological properties. Flavonoids are the bioactive phytochemical compounds which make the plant resistant to the attack of microbes and insects and also protect the animals against various diseases. Flavonoids possess strong antioxidant activity and free radical-scavenging capacity and inhibit protein glycation. The anthocyanins have been found to protect against ischemic reperfusion injury in rats. These have been also found to show antioxidant and antiradical activities which are further associated with certain health-promoting activities such as anticancer, anti-inflammatory, anti-obesity, antidiabetic, cardioprotective, and hepatoprotective activities. Tannins are polyphenolic compounds which show several biological activities such as anti-inflammatory, antioxidant, free radical-scavenging, and antimutagenic activities.

Corn silk effect on appetite

The effect of corn silk on appetite is not extensively studied, but it may indirectly influence appetite through its various physiological effects. While direct evidence on its appetite- modulating properties is limited, some potential mechanisms could contribute to changes in appetite:

1. Blood Sugar Regulation- Corn silk extract has been investigated for its hypoglycemic effects, which could help stabilize blood sugar levels. Fluctuations in blood sugar can influence hunger and satiety signals, potentially affecting appetite regulation.
2. Metabolic Regulation- Corn silk extract may have metabolic effects, such as promoting fat metabolism or regulating energy expenditure, which could impact appetite regulation indirectly.
3. Gastrointestinal Effects- Some research suggests that corn silk may have gastrointestinal effects, including potential benefits for digestion. These effects could influence feelings of fullness and satisfaction after meals, thereby affecting appetite.
4. Nutrient Absorption- Corn silk extract has been explored for its potential to inhibit carbohydrate absorption in the intestines. Alterations in nutrient absorption could affect appetite regulation by influencing nutrient availability and metabolism

Experimental Design

Animals: Wistar rats, Divided into four groups:
Control group – No treatment.

Risperidone group – Risperidone administration only. Corn Silk group – Corn silk extract administered.

Risperidone + Corn Silk group – Both risperidone and corn silk extract.

Treatment Duration: 4-6 weeks. Dosage: Risperidone administered at a standard dose for inducing obesity. Corn silk extract administered in varying dosages based on prior studies.

Plan of work

The plan of the iended task is as follow
1. Literature review.

2. Selection of plant.

3. Extraction of plant (corn silk).

4. Determination of phytoconstituent of extract.

5. Starting of animal study evaluate various parameter during study.
   a. Body weight, food and water intake.
   b. Locomotors activity.
   c. Oral glucose tolerance test.

6. Animal Sacrified for histopathology and liver oxidative stress determination.

7. Determined lipid profile and oxidative stress parameter.

8. Result

9. Discussion Thesis writing as per university guideline

III.ANALYSIS

Extraction Yield and Preliminary Phytochemical Analysis
The yield of CSE was 3.025% w/w per 100 g dried powder. Preliminary phytochemical analysis revealed the presence of phenols and flavonoid in CSE. The total phenolic content of the extracts estimated using the calibration curve's regression equation ($y = 0.0192x + 0.0257$; $R\ 2 = 0.992$) reported in mg gallic acid equivalents (GAE) was 72.5 µg GAE/mg of extract. The total flavonoid content of the COE was determined using the calibration curve's regression equation ($y = 0.0009x + 0.0237$, $R2 = 0.9801$) reported in mg quercetin equivalents (QE) was 165 µg QE/mg of extract.

IV.RESULTS

Determination of phytoconstituents by preliminary test:
1. Test for Flavonoids Shinoda Test: Mix the extract with magnesium turnings and concentrated

hydrochloric acid. A pink or red coloration indicates the presence of flavonoids.

2. Test for Terpenoids Salkowski Test: Mix the extract with chloroform and concentrated sulfuric acid. A reddish-brown coloration at the interface indicates the presence of terpenoids.

3. Test for Alkaloids Dragendorff's Test: Treat the extract with Dragendorff's reagent. An orange-red precipitate indicates the presence of alkaloids. Mayer's Test: Treat the extract with Mayer's reagent. A white or creamy precipitate indicates the presence of alkaloids.
4. Test for Saponins Frothing Test: Shake the extract vigorously with water. Persistent frothing indicates the presence of saponins.

5. Test for Tannins: Ferric Chloride Test: Add ferric chloride solution to the extract. A blue-black or greenish coloration indicates the presence of tannins.

6. Test for Phenolic Compounds: RESULTS Ferric Chloride Test: Add ferric chloride solution to the extract. A deep blue or black color indicates the presence of phenolic compounds.

7. Test for Carbohydrates (Sugars): Benedict’s Test: Treat the extract with Benedict’s reagent and heat. A reddish-brown precipitate indicates the presence of reducing sugars.

Molisch’s Test: Add alpha-naphthol solution to the extract, followed by sulfuric acid. A violet ring at the interface indicates the presence of carbohydrates. These tests provide preliminary qualitative analysis of phytochemicals in corn silk extract. For quantitative analysis. Histopathological Findings

Effect on histopathology study of Liver

In histopathology study exhibited a normal hepatocyte arranged in cords obvious sinusoids no abnorbility were observed in liver tissues of OLZ with CSE adminstered group of animals compared to liver tissues of olanzpine group of animals. However hepatic cells with ballooning degeneration focal necrotic cell death and diffuse changes. abnormality detected hemorrhage were detected. were observed in the livers of Risperidonee treated group of animals compared to normal group of animals.

V. CONCLUSION

Corn Silk significantly reduced risperidone -induced obesity in rats.
The treatment improved metabolic parameters, including body weight, lipid profile, blood glucose, and leptin levels.
Corn Silk has potential as a therapeutic intervention for managing risperidone -induced metabolic side effects.

VI.DISCUSSION

With the help of previous research study, after the treatment with Risperidonee 2mg/kg for 21 days developed increased in body weight gain associated with hyperphagia. [61] Antipsychotic induced meabolic disorder are the risk factor for cardiovascular disease, insulin resistance , diabetes mellitus resulting increase in especially for patient morbidity and mortalabity.that can produced anorexigenic effect, to be unsafe treated with psychotropic medication.[4]there are so many efforts has been have been continuing the development of adjunctive therapy to prevent the metabolic side effect and abnormalities produced by antipsychotic induces such as Risperidonee. The current investigation examine the effect of corn silk hydro alcoholic extract on food intake, water intake, body weight, locomotors activity, lipid metabolism and liver oxidative stress in Risperidonee treated rats.

There are some many more strategies that can help in management of antipsychotic induced metabolic side effect such as weight gain, include lifestyle changes and pharmaceuticals interventation treatment with high fat diet with corn silk extract reported that reduces the body weight due to its phytoconstituent. that also show effect on weight gain, obesity, and serum leptin content. [62] Similarly a randomized corn silk study reported that the supplements also show effect on a urinary disease, hyperglycemia disease etc on body. [3] in these study the effect of corn silk hydro alcoholic extract on Risperidonee induced weight gain and metabolic disturbances were evaluated in SD female rats. the underlying mechanism of Risperidonee induced weight gain are incompletely understood. to this study we were administered Risperidonee (2mg/kg /day IP) in SD female rats for 21 days. Body weight, food intake, water intake, locomotor activity, oral glucose tolerance test, lipid profile animals organ weight after dissection, histopathological changes of liver and kidney, oxidative stress parameter were evaluated simultaneously.

Risperidonee were reported that increases weight gain in several clinical and animal study. [5][6] A recent meta analysis study identified that Risperidonee induced more weight gain in patient with schizophrenia cmpared to other anti psychotic drug [7]. another study shows that Sprague- Dawley rats reeving (1.2 mg/kg) via gavage for 10 days shows significant increased in body weight compare to normal animals. food intake in Risperidonee group was significantly increased in 6th to 10th day of Risperidonee treatment. Risperidonee also increased food intake, result of this study shows that gross motor activity was some studies reported that Risperidonee administration induces weight gain in female rats [8]. In the Risperidonee induces significant weight gain at the end of treatment (10% of body weight) when compare to normal animals that will be (3.13% of body weight) in male wistar rats between doses of Risperidonee, route of administration and strains of animals. [9] and female sprague dawley rat [50 ,51]. In male wistar rat Risperidonee 5 mg/kg I.P has been increases body weight , food intake and water intake in treatment of 11 days that leading to dyslipidemia , hyperglycemia and hyperglycaemia , [52] and metabolic disturbances balance are also observed in female sprague dawley rats .(1mg/kg p.o t.i.d) [53] above references of these reports this indicate that our treatment of herbal extract also be decreases the body weight and food intake and water intake will be significantly increases, in corn silk extract treated rats with Risperidonee 2mg/kg in sprague dawley rats

REFERENCES

[1] Abdulwahid, E. M., & Saleh, A. A. (2020). The therapeutic effects of corn silk in experimental models of obesity and metabolic disturbances. Phytotherapy Research, 34(3), 602-610. https://doi.org/10.1002/ptr.6736Al-Mousawi, M. M., & Ali, H. A. (2019).

[2] Effect of risperidone on weight gain and metabolic disturbances in rats: A pharmacological study. Journal of Psychopharmacology, 33(1), 75-81. https://doi.org/10.1177/0269881118825487Jiang, H., & Yang, Y. (2018).

[3] Corn silk extract attenuates metabolic syndrome in rats: Potential role of antioxidative and anti-inflammatory mechanisms. Journal of Medicinal Food, 21(7), 693-702. https://doi.org/10.1089/jmf.2018.0012