IJPSR (2021), Volume 13, Issue 2 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 01 February 2021; received in revised form, 17 June 2021; accepted, 21 June 2021; published 01 February 2022

RUTIN - A POTENTIAL BIOFLAVONOID WITH VARIOUS PHARMACOLOGICAL ACTIONS

Pathivada Manasa and Ganta Suhasin *

Department of Pharmacology, GITAM Institute of Pharmacy, GITAM, Deemed to be University, Visakhapatnam - 530045, Andhra Pradesh, India.

Keywords:

Rutin, Flavonoid, Bioflavonoid, Metals, Chronic Diseases, Pharmacological properties.

Correspondence to Author:
Dr. G. Suhasin

Assistant Professor,
Department of Pharmacology,
GITAM Institute of Pharmacy,
GITAM, Deemed to be University,
Visakhapatnam - 530045, Andhra Pradesh, India.

E-mail: pathivada92@gmail.com

ABSTRACT: Rutin or quercetin-3-O-rutinose ($C_{27}H_{30}O_{16}$) is an essential member of the flavonoid family, a classification of total components of plant phenolic compounds. Rutin is typically located in buck herb seeds. Broccoli fruits, especially citrus fruits, red apples, and berries and drinks such as beer, tea, and coffee. This bioflavonoid is accountable for imparting color and flavor to fruits and vegetables. Rutin is located in many other plants, such as participants of the *Fagopyrum genera*, *F tataricum*, usually regarded as tartarine buckwheat, is specifically prosperous in protein. It works as a coloring agent, meal, additive, and used in cosmetics. Also, rutin has a more potent therapeutic effect than other flavonoid derivatives and therefore it is used as a medication to deal with vascular diseases. Several metals such as mercury, aluminum, titanium, vanadium and nickel can be determined spectroscopically by rutin. Rutin incorporates a broad range of pharmacological properties. Traditionally, it is used as anti-microbial, anti-fungal, and anti-allergic agents. However, the contemporary study proved its multi-spectrum pharmacological benefits for treating several chronic diseases, such as cancer, diabetes, high blood pressure, and excessive cholesterol.

INTRODUCTION: Rutin or quercetin-3-O-rutinose ($C_{27}H_{30}O_{16}$) is an important flavonoid family, a class of chief components of plant phenolics [1].

Structure and Chemical Properties of Rutin[1]:

- Chemical formula $C_{27}H_{30}O_{16}$
- Molar mass = 610.52 $g.mol^{-1}$
- Appearance = solid
- Melting point = 2420C (4680 F, 515 K)
- IUPAC Name: 2-(3,4-dihydroxy phenyl)-5,7-dihydroxy-3- [α-L-rhamnopyranosyl -(1→6)-β-D-glucopyranosyloxy] -4H-chromen-4-one

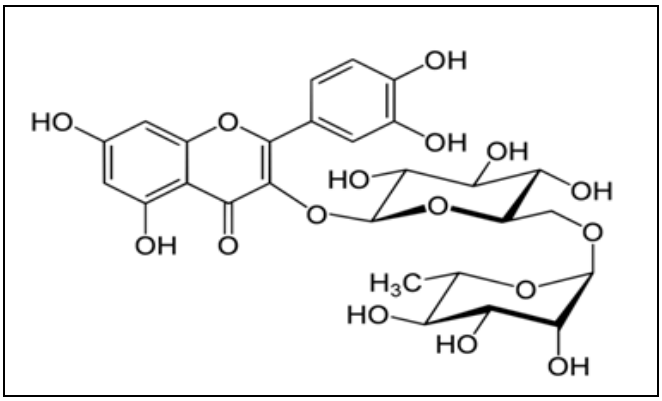

FIG. 1: CHEMICAL STRUCTURE OF RUTIN

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.13(2).598-02

This article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.13(2).598-02

Biological Sources of Rutin: Rutin is commonly found in buck herb seeds. Broccoli fruits, especially citrus fruits, red apples and berries and beverages such as beer, tea and coffee. This bioflavonoid is responsible for imparting color and flavor to fruits and vegetables [2]. Rutin is also found in many other plants, such as *Fagopyrum genera* members. *F. tataricum*, commonly known as tartarine buckwheat, is particularly rich in protein. Dry buckwheat seeds contain up to 1.7 percent of rutin. In comparison, the common buckwheat seed, scientifically known as Fagopyrum esculentum, has only 0.01% of the rutin by dry weight. Rutin is also found in citrus fruits like oranges, lemons, limes, and grapefruit. Apples are full of routine. Buckwheat, most citrus fruits, figs, and black and green tea also contain rutin.

Biological Uses: It acts as a coloring agent, food additive, and used in cosmetics. Also, rutin has a more potent therapeutic effect than other flavonoid derivatives. Therefore it is mainly used as a medicine to treat vascular diseases [3]. Several metals such as mercury, aluminum, titanium, vanadium, and nickel can be determined spectroscopically using rutin. Its structural composition forms complexes with metal cations only and can also form stable complexes with metal oxy-ions. The rutin structure contains multiple hydroxyl groups **Fig. 1.** which form complexes with minerals and become the basis for rutin's determination from medicines, foods, and beverages. Rutin is a flavonoid, or vegetable dye, found in some vegetables and fruits. Apples are full of routine. Buckwheat, most citrus fruits, figs, and black and green tea also contain rutin.

Pharmacological Actions: Rutin contains a wide range of pharmacological properties. Conventionally, it is used as an anti-microbial, anti-fungal, and anti-allergic agent. The present focuses on the pharmacological potentials as studied in various experimental models in the past few years [4].

TABLE 1: RUTIN PHARMACOLOGICAL ACTIONS

S. no.	Pharmacological activities	Reference
1	Central nervous system	1
2	Sedative activity	2
3	Anticonvulsant activity	3
4	Anti-Alzheimer activity and treatment of hyperkinetic movement disorder	4
5	Antidepressant effects	4
6	Analgesic and anti-arthritic activities	5
7	Analgesic and antinociceptive effects	6
8	Anti-arthritic effects	7
9	Antidiabetic effects	7
10	Anti-hypercholesterolemic effects	9
11	Antiulcer effects	9
12	Antiosteoporotic and antiosteopenic effect	9
13	Anticataract and ophthalmic effect	9
14	Diuretic effect	9
15	Reproductive system Effect on sperm quality and male reproductive organs	11
16	Anticancer effects	12
17	Antibacterial activity	12
18	Anti-fungal activities	13
19	Antimycobacterial activity	13
20	Larvicidal activity	14
21	Antimalarial activity	14
22	Antiretroviral activity	15
23	Antiviral activity	16
24	Anti-fatigue activity	17
25	Retinoprotective activity	18
26	Cardioprotective effects	19
27	Prevention of splenocyte apoptosis	20
28	Hepatoprotective activity	20

Prevention of Neuro-inflammation: Rutin demonstrated a Neuroprotective effect on cerebral ischemia. Rutin administration caused impairment of "ischemic neuron apoptosis" due to embarrassment of p53 expression and lipid peroxidation and increased "antioxidant self-defense enzymes" [5].

It is helpful in hypoxic, glutamate, and oxidative stress. Reduction of 'neuron Flammarion' in a rat model of 'sporadic dementia of Alzheimer type and Neuroprotective effects in 'dexamethasone-treated mice' was observed rutin administration.

Promote Neural Crest Cell Survival: The neural crest is an ancestor consisting of neuro potential and medium voltage. The treatment of rutin to the stem cell of neuronal apex improved its viability without altering cell differentiation that might be due to modulation of ERK2 and PI3K pathways [6].

Sedative Activity: Rutin's CNS and behavioral training had been on thiopental-induced sleeping time and locomotor activity tests in mice. Rutin administrated intra peritoneal induced depressant motion on the central nervous system. The research confirmed rutin's CNS depressant activity was unlikely due to the GABAa receptors involvement [7].

Anticonvulsant Activity: Rutin also possesses anticonvulsant activity and appears to be secure for patients with epilepsy. It does not alter the exercising of any of the administered antiepileptic drugs or demonstrates any adverse effects.

Analgesic and Antinociceptive Effects: Rutin's analgesic effect was studied through the hot plate test on Swiss albino mice, whereby rutin analgesic impact was once established. Moreover, it was once additionally proven that rutin exhibited peripheral and central antinociceptive activities [8].

Anti-Arthritic Effects: Animals treated with rutin were determined with an extensive decrement in rheumatoid arthritis and Fanconi anemia using 'oxygen radical overproduction.' In the rat model of arthritis, rutin prevented the acute and persistent degrees of inflammation. Rutin used to be most energetic in the chronic phase of inflammation. In an adjuvant arthritis rat model, rutin inhibited acute and chronic phases of inflammation. Rutin was the most active in the chronic stage of infection. Due to anti-fungal and anti-arthritic effects, rutin has a therapeutic impact on septic arthritis caused by Candida albicans. Moreover, in an independent study, rutin of inflammatory and catabolic markers was slowed down in osteoporotic lesions of Hartley's guinea pigs [9].

Anti Diabetic Effects: In the study, chronic rutin administration in streptozotocin-induced diabetes mice caused a reduction in plasma glucose, improved insulin levels, and restored glycogen content and glucose-degrading enzymes. Significant regeneration of islets of the pancreas with decreased lipid infiltration was determined in rutin-treated diabetic mice. Reduced fasting plasma glucose levels, glycosylated hemoglobin, peptide c, and malondialdehyde have been discovered in mice treated with streptozotocin and diabetes [10]. Rutin averted the ranges of enzymes *viz.* ALT, AST, and LDH in the serum, liver, and coronary heart show a protecting effect on hepatic and cardiac toxicity related due to streptozotocin. Alteration in matrix metalloproteinase activity and safety to the kidney against streptozotocin-induced damage used to be observed [11]. Rutin encouraged glucose uptake in the soleus muscle, and the impact used to be mediated *via* extracellular calcium and calcium-calmodulin-dependant protein kinase II activation. An increase in intracellular calcium attention is involved in DNA activation, which rutin moderated. Rutin added for glycemic management with the aid of enhancement of insulin receptor kinase activity, as a result, ' insulin signaling pathway' that triggered which increases the GLUT4 translocation and augmented glucose uptake [12].

Anti-Ulcer Effects: A peptic ulcer is an infirmity that influences the substantial population in the world. Ulcers are found when disparity occurs among 'aggressive' and 'protective' factors at the luminal surface of the gastric epithelium. HCL, pepsins, non-steroidal anti-inflammatory drugs, Helicobacter pylori, bile acids, ischemia, hypoxia, smoking, alcohol, *etc.*, consists of dynamic elements, whereas defensive factors comprise bicarbonate, a mucus layer, mucosal blood flow, P.G.s and growth factors.

Antiasthmatic Activity and Other Associated Effects: The antiasthmatic activity of rutin was studied in ovalbumin sensitized conscious guinea-

pigs challenged with aerosolized ovalbumin where airway resistance occurs during the immediate phase and late-phase response used to be determined.

Rutin substantially inhibited specific airway resistance and immediate-phase response along with the resistance of histamine, phospholipase A2 and eosinophil peroxidase. There was reduced conscription of neutrophils and eosinophils into the lung. Use of rutin was additionally recommended in whooping cough along with nutritional vitamins C and K. In cats and whippets; rutin has been effectively used in the management of idiopathic chylothorax [13].

Diuretic Effect: Quercetin, a metabolite of rutin, which is abundantly determined in hibiscus sabdariffa Linn acted on vascular endothelium, causing nitric oxide release, leading to growing renal vasorelaxation through developing kidney filtration [14].

Reproductive System: Rutin, in a study, afforded to protect effect on damage to human sperm precipitated using lipid peroxidation. Rutin additionally demonstrated safety to testicular tissue and reproduction from oxidative stress found in type 1 diabetes mellitus along with amelioration of cyclophosphamide-induced reproductive toxicity and testicular ischemia-reperfusion-induced oxidative stress in rats [15].

Neuroprotective Activity: In the mice model, rutin inhibited oxaliplatin-induced chronic painful peripheral neuropathy. Oxaliplatin is one of the essential platinum compounds used in colorectal cancer chemotherapy.

However, it suffers from a drawback of peripheral, which seems to be challenging to treat. Rutin significantly decreased oxaliplatin-induced peroxidative changes in the spinal cord and lipid peroxidation along with inducible nitric oxide [16].

Retinoprotective Activity: Effect of rutin on ocular blood flow by ‘colored microsphere technique' was determined. Electro-retinography was used to determine the b-wave recovery, a tool for estimation of retinal function recovery. Rutin increased ocular blood flow and demonstrated a remarkable effect on retinal function recovery [17].

Pharmacokinetics:

Absorption: Rutin can attach to and traverse the small intestine. of The binding flavonoids to the intestinal wall components limits their absorption from the small intestine [18].

Metabolism: Metabolites are 3, 4- di hydroxyl phenylacetic acid, 3, 4-dihydroxytoluene, m-hydroxy phenylacetic acid, 3-methoxy-4- hydroxyl phenylacetic acid/homo vanillic acid, and quercetin [19].

Excretion: About 10% in urine, rest unchanged in feces [20].

CONCLUSION: Rutin has a wide range of pharmacological properties. However, the current study has shown its multi-spectrum pharmaco-logical benefits for treating various chronic diseases, such as cancer, diabetes, high blood pressure, and high cholesterol.

ACKNOWLEDGEMENT: I would like to express my genuine thanks to Dr. G. Suhasin, Assistant Professor, GITAM Institute of Pharmacy, for giving me this opportunity to carry out my study in the GITAM (Deemed to be University) Visakhapatnam.

CONFLICTS OF INTEREST: All authors declared that there are no conflicts of interest.

REFERENCES:

1. Alvarez-Mon MA, Gómez AM, Orozco A, Lahera G, Sosa MD, Diaz D, Auba E, Albillos A, Monserrat J and Alvarez-Mon M: Abnormal distribution and function of circulating monocytes and enhanced bacterial translocation in major depressive disorder. Front Psychiatry 2019; 10: 812.
2. Becker RC, Owens AP and Sadayappan S: Tissue-level inflammation and ventricular remodeling in hypertrophic cardiomyopathy. J Thromb Thrombolysis 2020; 49: 177-83.
3. Chiu YJ, Hsieh YH, Lin TH, Lee GC, Hsieh-Li HM, Sun, YC, Chen CM, Chang KH and Lee-Chen GJ: Novel compound VB-037 inhibits Aβ aggregation and promotes neurite outgrowth through enhancement of HSP27 and reduction of P38 and JNK-mediated inflammation in cell models for Alzheimer’s disease. Neurochem Int 2019; 125: 175-86.
4. Colmorten KB, Nexoe AB and Sorensen GL: The dual role of surfactant protein-d in vascular inflammation and development of cardiovascular disease. Front Immunol 2019; 10: 2264.
5. Domingos ODS, Alcântara BGV, Santos MFC, Maiolini TCS, Dias DF, Baldim JL, Lago JHG, Soares MG and Chagas-Paula DA: Anti-Inflammatory derivatives with

dual mechanism of action from the metabolomic screening of *Poincianella pluviosa*. Molecules 2019; 24: 4375.
6. Dymarska M, Janeczko T and Kostrzewa-Susłow E: Glycosylation of methoxylated flavonoids in the cultures of isaria fumosorosea KCH J2. Molecules 2018; 23: 2578.
7. He J and Yang B: Aquaporins in renal diseases. Int J Mol Sci 2019; 20(2): 366.
8. Justino AB, Costa MS, Saraiva AL, Silva PH, Vieira TN, Dias P, Linhares CRB, Dechichi P, de Melo Rodrigues Avila V, Espindola FS: Protective effects of a polyphenol-enriched fraction of the fruit peel of *Annona crassiflora* Mart. on acute and persistent inflammatory pain. Inflammo Pharmacology 2019.
9. Kaptoge S, Pennells L, De Bacquer D, Cooney MT, Kavousi M, Stevens G, Riley LM, Savin S, Khan T, Altay S: World health organization cardiovascular disease risk charts: revised models to estimate risk in 21 global regions. Lancet Glob Health 2019; 7: e1332-e45.
10. Kuznetsova T, Prange KHM, Glass CKCK and de Winther MPJ: Transcriptional and epigenetic regulation of macrophages in atherosclerosis. Nat Rev Cardiol 2019.
11. Lima TS, Gov L and Lodoen MB: Evasion of human neutrophil-mediated host defense during toxoplasma gondii infection. M Bio 2018; 9: 02027-17.
12. Melnikov IS, Kozlov SG, Saburova OS, Avtaeva NY, Prokofieva LV and Gabbasov ZA: Current position on the role of monomeric C-reactive protein in vascular pathology and atherothrombosis. CPD 2019: 25.
13. Mendes LF, Gaspar VM, Conde TA, Mano JF and Duarte IF: Flavonoid-mediated immunomodulation of human macrophages involves key metabolites and metabolic pathways. Sci Rep 2019; 9: 14906.
14. Murray PJ: Immune regulation by monocytes. Semin Immunol 2018; 35: 12-18.
15. Najmanová I, Vopršalová M, Saso L and Mladˇenka P: The pharmacokinetics of flavones. Crit Rev Food Sci Nutr 2019: 1-17.
16. Ortega MA, Asúnsolo Á, Leal J, Romero B, Alvarez-Rocha MJ, Sainz F, Álvarez-Mon M, Buján J and García-Honduvilla N: Implication of the PI3K/Akt/mTOR pathway in the process of incompetent valves in patients with chronic venous insufficiency and the relationship with aging. Oxidative Med Cell Longev 2018: 1-14.
17. Ortega MA, Asúnsolo Á, Romero B, Álvarez-Rocha MJ, Sainz F, Leal J, Álvarez-Mon M, Buján J and García-Honduvilla N: Unravelling the role of mapks (erk1/2) in venous reflux in patients with chronic venous disorder. Cells Tissues Organs 2018; 206: 272-82.
18. Saha S, Panieri E, Suzen and S Saso L: The interaction of flavonols with membrane components: potential effect on antioxidant activity. J Membr Biol 2020; 253: 57-71.
19. Sieve I, Ricke-Hoch M, Kasten M, Battmer K, Stapel B, Falk CS, Leisegang MS, Haverich A, Scherr M and Hilfiker-Kleiner D: A positive feedback loop between IL-1β, LPS and NEU1 may promote atherosclerosis by enhancing a pro-inflammatory state in monocytes and macrophages. Vasc. Pharmacol 2018; 103-05: 16-28.
20. Vogel S and Thein SL: Platelets at the crossroads of thrombosis, inflammation and haemolysis. Br J Haematol 2018; 180: 761-67.

How to cite this article:
Manasa P and Suhasin G: Rutin - a potential bioflavonoid with various pharmacological actions. Int J Pharm Sci & Res 2022; 13(2): 598-02. doi: 10.13040/IJPSR.0975-8232.13(2).598-02.