IJPSR (2023), Volume 14, Issue 9 (Review Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 02 January 2023; received in revised form, 21 March 2023; accepted 30 May 2023; published 01 September 2023

THE PHARMACOLOGICAL ACTIONS OF IRIFLOPHENONE-3-C-β-D GLUCOSIDE: AN OVER VIEW

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Keywords:

Iriflophenone 3-C-β-D glucoside, Antidiabetic, Antioxidant, Antibacterial, Anti-inflammatory, Anti- proliferative

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ABSTRACT: Iriflophenone 3-C-β-D glucoside is a Benzophenone derivative which can be obtained from various plant sources like *Aquilaria crassna, A. sinensis, A. malaccensis, Cyclopia genistoides, Mangifera indica, Dryopteris ramosa etc*. It can act as an important herbal active constituent as it has various pharmacological actions, such as Antidiabetic, anti-inflammatory, antioxidant, and antimicrobial agent. Some scientists demonstrated the antioxidant activity of Iriflophenone 3-C-β-D glucoside and have seen that this compound has no radical scavenging ability against DPPH [2,2-diphenylpicrylhydrazyl] but scavenged ABTS [2,2'-azino-bis(3- ethylbenzothiazoline-6-sulphonic acid)] and peroxyl radicals. So, it can be used as an anti- oxidant agent. From *A. sinensis* 8 compounds were isolated among which Iriflophenone 3-C- β-D glucoside was present. It is proved that all the isolated compounds have α-glucosidase inhibition activity stronger than acarbose, that is taken as positive drug control. Aqueous fraction of *D. ramosa* is used for so long by the inhabitants of the Galliyat region of Pakistan to treat their GIT ailments caused by bacteria. Scientists showed that Iriflophenone 3-C-β-D glucoside that is obtained from *Dryopteris ramosa* has stronger antibacterial potential against *Klebsiella pneumoniae, Staphylococcus aureus,* and *Escherichia coli.* The anti-inflammatory activities of this compound are revealed as the aqueous extract of *A. crassna* expressed strong IL-1α and IL-8 inhibitions and the 70% Ethanolic extract showed IL-1α and NO inhibitions. Apart from this there are many other effects of that compound which are still under research. Such versatile uses make this compound a highly valuable herbal constituent.

INTRODUCTION: Iriflophenone 3-C-β-D glucoside is a Benzophenone derivative. The IUPAC name of this compound is (4-hydroxyphenyl) - [2, 4, 6 – trihydroxy – 6 - (hydroxyl-methyl) oxan – 2 - yl] phenyl] methanone. The molecular weight of this compound is 408.4 g/mol. This compound is obtained through the shikimic acid pathway.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.14(9).4384-92

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

DOI link: http://doi.org/10.13040/IJPSR.0975-8232.14(9).4384-92

This compound can be obtained from various plant sources like *Aquilaria crassna, A. sinensis, A. malaccensis, Mangifera indica, Dryopteris ramosa, Cyclopia genistoides etc.*

As it is a secondary metabolite, it can be obtained in different plant parts like leaf, seed, bark *etc.* though the content in each part will be different. It is found in a very less amount. Still, it can act as an important herbal active constituent as it has various pharmacological actions it can act as Antidiabetic, anti-inflammatory, antioxidant, antimicrobial agent and apart from this, it also has also an activity on reduction of cholesterol [1, 2]. The thermal degradation kinetics and pH rate profile were

demonstrated by Wongwad *et al.* [3] and showed that the degradation of this compound follows the first-order kinetic reaction. According to the first-order kinetic studies the predicted shelf life of this compound at 25°C in pure form is 248 days with an activation energy 110.57 kJ/mol. So, as it has optimum thermal stability, it can be used to develop different formulations as an active ingredient. The pharmacological actions of this compound that are found in various research articles are written below-

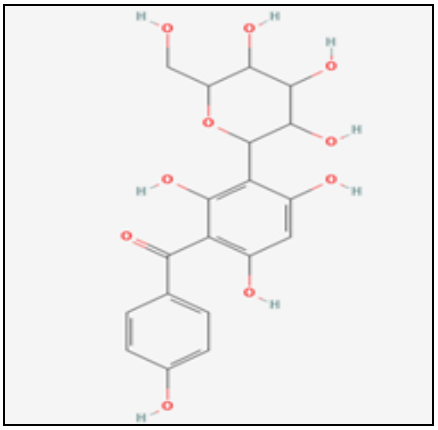

FIG. 1: STRUCTURE OF IRIFLOPHENONE 3-C-B-D GLUCOSIDE (Source: National Center for Biotechnology Information. Pubchem Compound Summary for CID 53396784, Iriflophenone-3-C-β-D-glucopyranoside. https://pubchem.ncbi.nlm.nih.gov/compound/Iriflophenone-3C-beta-D-glucopyranoside. Accessed Dec. 31, 2022.)

Antibacterial Effect: Chemical compounds obtained from plants generally have a great structural diversity and enact important precursor compounds to develop new restorative agents. Generally, the evolutionary selection pressure produces diversity in plant phytochemicals. *Dryopteris ramosa* C. Chr. Is a common fern plant found in Galliyat region of Pakistan [4].

It belongs to the plant family Dryopteridaceae. There are various researches on the pharmacological actions of *D. ramosa*. Some ethnopharmacologists find that the aqueous fraction of *D. ramosa* can be used as gastrointestinal tonic [4] to cure stomach pain [5] and treat gastric ulcers and constipation. It also has antimicrobial as well as anti-cancer and antioxidant potential. This plant is traditionally used in the Galliyat region of Pakistan to treat gastrointestinal tract ailments that are especially caused by bacteria. Ishaque *et al.* [6] have isolated the bioactive compound Iriflophenone 3-C-β-D glucoside that has antibacterial potential against five bacterial strains and compared it with a known antibiotic Cefixime. The Brine Shrimp Lethality Test (BSLT) test is used to determine the cytotoxicity. Iriflophenone 3-C-β-D glucoside has shown a strong anti-bacterial potential (MIC = 31.1 ±7.2, 62.5 ± 7.2, and 62.5 ±7.2 g/mL) against *Klebsiella pneumoniae*, *Staphylococcus* aureus, and *Escherichia coli*, respectively. On the other hand, the least antibacterial potential is shown by Iriflophenone 3-C-β-D glucoside (MIC = 125 ± 7.2 g/mL), against *Bacillus subtilis*, in comparison to Cefixime (MIC = 62.5 ±7.2 g/mL). The cytotoxicity of Iriflophenone 3-C-β-D glucoside is significantly low (LD50 = 10.037 ±2.8 g/mL) against *Artemia salina nauplii*. This study justified the ethnomedicinal use of *D. ramosa* and the importance of ethnomedicinal knowledge about it.

Antidiabetic Activity: Aquilaria or agarwood leaves have been found to have various biological activities. Feng *et al.* [7] performed an alpha-glucosidase inhibition assay to isolate active compounds present in *Aquilaria sinensis* [8]. Eight compounds are isolated those are aquilarisinin, aquilarisin, aquilarixanthone, hypolaetin 5-O-β D-glucopyranoside, Iriflophenone 3-C-β-D gluco-pyranoside, Iriflophenone 3,5-C-β- diglucopy-ranoside, mangiferin, Iriflophenone 2-O-α-L – rhamnopyranoside. All isolated compounds exhibit α-glucosidase activity [9] stronger than acarbose, which is used as a positive drug control in STZ induced diabetic mice.

These polyphenolic compounds inhibit α-glucosidase and prevent the digestion and absorption of carbohydrates [10]. α- glucosidase inhibition does not affect the glucose that has already been absorbed into the body. However, the activity of the compounds (except mangiferin) in regulating glucose disposition in the peripheral tissues is not yet investigated [11]. This type of activity is one of the actions of antidiabetics. The structure-activity relationships of polyphenolic compounds are well established for inhibiting the enzyme α- glucosidase, leading to an anti-hyperglycaemic effect [12, 13].

Pranakhon *et. al.* [9, 14] has investigated that Iriflophenone 3-C-β-D glucopyranoside can lower the fasting blood glucose level, has a good

antidiabetic potential compared to Insulin, and has lipid-lowering activity [15].

Fasting Blood Glucose Lowering activity of the Methanolic Extract and Iriflophenone 3-C-β-D Glucopyranoside: The weight of the mice used in this study= 25-35 g. The STZ-induced diabetic mice that were treated with distilled water lost significant weight (12.8% ± 2.3%). This weight loss is a sign of diabetes.

The STZ-induced diabetic mice that were treated with Iriflophenone 3-C-β-D glucoside (IPG) and Insulin did not display any changes in weight from the start of the treatment. On the other hand, treatment with the Methanolic Extract showed a drastic weight loss of −24.7% ± 2.6%. It is shown that the fasting blood glucose levels of the group of mice treated with 1.0 g/kg ME and 0.47 g/kg IPG (reduced blood glucose by 40.3% and 46.4%) were nearly similar to those of the group treated with 8 U/kg insulin (41.5%).

Effects of Iriflophenone 3-C-β-D Glucoside on Glucose Uptake into Adipocytes of Rat: The increase in glucose uptake into rat adipocytes by treatment with 0.25 and 2.5 μM IPG was 153.3% and 154.6%, respectively. These enhancements were about the same as that resulting from treatment with 1 mg/L of ME (152%), while the effect shown by treatment with 1.5 nM insulin was 183% which is very much high. At IPG doses of 12.5 and 25 μM, glucose uptake was increased to approximately 114-117% which was 11-14% above that of the negative control (Krebs-Ringer-Bicarbonate-Buffer). Thus, the minimum concentration of IPG that exerts the highest effect is 0.25 μM.

Saleem *et al.* [16] have done a study that evaluates the potential of mango leaves for their use against Diabetes Mellitus. The hydroalcoholic mixture of *Mangifera indica* was prepared by them and which is evaluated by High performance liquid Chromatography. The chemical evaluation showed the presence of Iriflophenone 3-C- β-D glucoside and other polyphenolic and Benzophenone compounds. The results have shown a decrease in post-prandial glucose following seven days of therapy in diabetic mice [11]. Apart from this the extract also prevented the rice in blood glucose level as determined by glucose tolerance test in diabetic mice. Furthermore, the extract prevented a decrease in body weight.

Anti-inflammatory Property: Wongwad *et al.* [17] showed that *Aquilaria crassna* is a potential source of natural ingredients for anti-inflammatory drugs and anti-aging cosmetics. The anti-inflammatory activities are revealed as the aqueous extract expressed strong IL-1α and IL-8 inhibitions, while the 70% ethanolic extract showed IL-1α and NO inhibition. *A. crassna* Pierre ex Leomte is a highly valuable medicinal plant that belongs to the family Thymelaeaceae [18]. Found in the rainforests throughout Southeast Asia. In, Thailand *A. crassna* leaves are being traditionally used in herbal tea to treat various disorders of the heart and blood circulatory systems [19]. Numerous chemical constituents are found in *A. crassna* like Phenolic acids, steroids, terpenoids, pyranones, quinones, Benzophenones, xanthonoids, flavonoids and nucleosides [20].

But the main compounds of interest in that study are Iriflophenone 3,5-C-β-D diglucoside, (i) Iriflophenone 3-C-β-D glucoside (ii), mangiferin (iii), genkwanin 5-o-β-primevoside (iv). These 4 compounds can have various effects like neuroprotection, [21] anti-inflammatory, antioxidant, [22] anti-hyperglycaemic, antibacterial [23,] *etc*. These study aims to explore the possibility of using A. crassna leaves in the cosmeceutical industry.

The aqueous and 70% Ethanolic extracts of young leaves of *A. crassna* are studied in that research for determining anti-inflammatory activity [24]. The anti-inflammatory activities of the extracts were evaluated through the inhibition of interleukin-1α (IL-1α), interleukin-8 (IL-8), and prostaglandin E2 (PGE2) that are secreted from human keratinocyte cells after UVB irradiation [25]. Furthermore, the extracts are also evaluated through nitric oxide (NO) inhibition on lipopolysaccharide (LPS)-stimulated macrophage cells and lipoxygenase (LOX) inhibition using red ferric thiocyanate (FTC) assay [26].

Result of Anti-inflammatory Activity Determined in *A. crassna* leaves: Keratinocyte and Macrophage Cells Viability: In Keratinocyte and macrophage cells viability [27] study,

Keratinocyte and macrophage cells are treated with different concentrations of aqueous extract, 70% ethanolic extract and also compounds (i–iv) that are Iriflophenone 3,5-C-β-D diglucoside (i) Iriflophenone 3-C-β-D glucoside (ii), mangiferin (iii), genkwanin 5-o-β-primevoside (iv) respectively. After the cells were treated with those extracts for 24 h, the number of surviving cells was determined using MTT assay. The results showed that aqueous and 70% ethanolic extracts significantly decreased the keratinocyte cell viability, relative to the control, when concentrations were increased to 25 and 50 µg/mL A similar result was found in a macrophage cell viability test. These results indicated that the safe concentration for further *in-vitro* investigation on human keratinocyte and macrophage cells should be lower than 25 µg/mL for both aqueous and 70% ethanolic extract.

Inhibition of IL-1α, IL-8 and PGE2: The effects of aqueous extract, 70% Ethanolic extract and also the compounds (i-iv) on IL-1α, IL-8 and PGE2 inhibition on UV-B induced human keratinocyte cells are tested and evaluated at the concentration of 10 µg/mL of each sample. The aqueous extract as well as the 70% Ethanolic extracts have shown strong IL-1α inhibitory activity and are significantly different from the control group (UV-B induced without treatment). Compounds (i) and (ii) have shown high inhibition on IL-1α compared with that positive control, dexamethasone, while compound (iii) has expressed moderate inhibition on IL-1α. However, no inhibition was seen in compound (iv). After the comparing the inhibition of IL-8 between the aqueous extract and the control group it was seen that the IL-8 inhibition was significantly stronger in aqueous extract than that of control group, while the other samples did not show any activity. The result also indicated that 70% ethanolic extract could stimulate the keratinocyte cells to secrete higher amounts of IL-8, as compared with the UVB-induced control group. The presence of other compounds in 70% ethanolic extract might be the possible cause of such effects.

The results showed that compounds (i–iv) inhibited PGE2 secretion as same as diclofenac. At the tested concentrations, the aqueous extract tended to inhibit the PGE2 secretion but the inhibition was not statistically significant. A higher concentration of the extract might need to be tested, but that lead to cause morphological changes and cell death which were observed from the preliminary cell viability test. Surprisingly, 70% ethanolic extract stimulated keratinocyte cells to secrete higher PGE2 production than the control group, indicating that 70% ethanolic extract might be harmful to the cells.

Antioxidant Activity: Malherbe *et al*. [28] isolated the Benzophenone Iriflophenone 3-C-glucoside from *Cyclopia genistoides* through fluid-fluid extraction, high-performance counter-current chromatography and high-performance and semi-preparative high-performance liquid chromatography. The Microplate Oxygen Radical Absorbance Capacity (ORAC) assay with fluorescein as probe is adapted for being used in online HPLC configuration. The method is validated using a mixture of authentic standards including Iriflophenone 3- C-glucoside and the xanthones, mangiferin and isomangiferin. They have also used Trolox (6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid) and included it in the mixture to determine the Trolox Equivalent Antioxidant Assay (TEAC) values. Through the use of online HPLC-ORAC assay, as well as 2,2-Diphenyl-1- picrylhydrazyl (DPPH) and 2,2'-azinobis-(3-ethylbenzothiazoline-6-sulphonic acid) (ABTS) online assays, Malherbe *et al.* demonstrated the antioxidant activity of Iriflophenone 3-C-glucoside and isomangiferin. Iriflophenone 3-C-glucoside has shown no radical scavenging ability against DPPH but scavenged ABTS and peroxyl radicals ($TEAC_{ABTS}$ of 1.04 and $TEAC_{ORAC}$ of 3.61).

Wongwad *et al.* [17] showed that *Aquilaria crassna* is a potential source of natural ingredients for preparing anti-aging cosmetics. Numerous chemical constituents are found in *A. crassna*, like Phenolic acids, steroids, terpenoids, pyranones, quinones, Benzophenones, xanthonoids, flavonoids and nucleosides [20] but the main compounds of interest in that study are Iriflophenone 3,5-C-β-D diglucoside (i), Iriflophenone 3-C-β-D glucoside (ii), mangiferin (iii), genkwanin 5-o-β-primevoside (iv). The aqueous extract and 70%methanolic extract of young leaves of *A. crassna* have an antioxidant potential [29]**,** mainly determined by the

DPPH and FRAP assay. Principal component analysis (PCA) is also used in this study to determine the antioxidant property of *A. crassna* leaves.

The Antioxidant Activity of *A. crassna* Leaf Extract through DPPH and FRAP Assay: The aqueous and 70% ethanolic extracts of both young and mature *A. crassna* leaves from different regions of Thailand, and the standard compounds (i–iv), were tested and evaluated for their antioxidant activity through DPPH and FRAP assays [30] and the results were compared with Trolox (positive control). The DPPH assay indicated that young leaf extracts from both solvents (aqueous, 70% Ethanolic) showed greater antioxidant activity when compared with mature leaf extracts. The IC_{50} values of the young leaves varying from 13.3 to 26.5 μg/mL, and the IC_{50} values of the mature leaves varying from 37.5 to 71.4 μg/mL. The IC_{50} values of the compounds (ii) and (iii) were 40.5 ±3.05 μg/mL and 7.7 ±0.20 μg/mL while the IC_{50} values of compounds (i) and (iv) were higher than 83 μg/mL. The positive control, trolox, showed IC_{50} of 5.4 ± 0.70 μg/mL.

It was seen that most of the 70% ethanolic extracts showed higher antioxidant activity via DPPH assay than the aqueous extracts of the same plants. The results of the FRAP assays were in agreement with those of the DPPH assays, with both the aqueous and 70% ethanolic extracts of the young leaves showing stronger antioxidant activity as compared with the mature leaf extracts, with reducing powers varying from 2.6 to 3.6 mmol Fe2+/g sample for the young leaf extracts and 0.9 to 1.5 mmol Fe^{2+}/g sample for the mature leaf extracts.

Compound (iii) showed the strongest activity with a reducing value of 10.5 ± 0.05 mmol Fe2+/g sample as compared with the Trolox 8.0 ± 0.19 mmol Fe2+/g sample. In contrast, compounds (i), (ii) and (iv) showed lower activity with reducing values of 0.2 ± 0.01, 1.2 ± 0.06 and 0.4 ± 0.03 mmol Fe2+/g sample, respectively. These results suggest that compound (iii) contributes to the antioxidant activity of the extracts. The amount of compound (iii) was high in the 70% ethanolic extracts of young leaves, which corresponds to the fact that these samples showed higher antioxidant activity than the mature leaves and the aqueous extracts of both young and mature leaves. The antioxidant activity of compound (iii) has also been noted in many other reports

PCA Analysis of 24 Samples of *A. crassna* Leaf Extracts based on the Contents of Compounds (i–iv) and the Antioxidant Activities: PCA is a technique used for multivariate analysis of data to reduce a dataset to the similar main components and has been frequently used in research studies such as to differentiate the chemical components from various sources of plants and to characterize plants for quality standardization. In their studies, PCA was applied to classify the *A. crassna* leaf extracts based on their contents of compounds (i–iv) and antioxidant activities (values obtained from FRAP assay are mmol Fe2+/g sample and that from DPPH assay are $1/IC_{50}$). Two principal components that revealed an accumulated variance of PC1 and PC2 which is 69.8% and 16.4% of the total variance, were chosen to construct a loading diagram. According to the factor score, the test samples were situated in a two-dimensional space, with some specific grouping.

These groups could be well explained based on the loading spots of the amount of chemical compounds (i–iv) and antioxidant activities from the DPPH and FRAP assays. The group consisting of 70% ethanolic extracts of *A. crassna* young leaves from all provinces, with the highest PC1 and PC2 scores, was characterized by high amount of compound (iii), accounting for 15–21%w/w.

Compound (i) was the most abundant component of the aqueous extract of *A. crassna* young leaves from all provinces, accounting for 13–21%w/w, and grouped these samples with high PC1 and negative PC2 scores. These aqueous and 70% ethanolic extracts of young leaves were also grouped with a high amount of compounds (i) (10 21%w/w), (ii) (0.6–4.6%w/w), (iii) (9–21%w/w) and high antioxidant activities (IC50 of 13.3–22.6 μg/mL for DPPH assay and 2.6–3.6 mmol Fe2+/g sample for FRAP assay). Another group consisted of 70% ethanolic extracts of mature *A. crassna* leaves from all provinces, characterized by high amounts of compound (iv) (0.2–6%w/w). The results obtained from PCA confirmed that both aqueous and 70% ethanolic extracts of young leaves show higher antioxidant activity than the

extracts from mature leaves. The higher antioxidant activity is associated with, the higher contents of compounds (i– iii) found in the young leaves.

Antihyperlipidemic Activity: High cholesterol is the 6th risk factor of death in the world in recent days [31]. Diets with high saturated fat, physical inactivity, and genetic consideration can increase cholesterol levels. Cholesterol can also increase the risk of other diseases like stroke, ischemic heart disease, atherosclerosis, and other cardiac complications. Individuals with elevated low-Density Lipoproteins (LDL) are prone to develop coronary heart disease. So, lowering LDL is the primary therapy to avoid other diseases. Various marketed drugs are used to lower cholesterol, mainly the LDL, like HMG Co-A reductase inhibitors [32] (example- Statins). But as these chemical drugs have various side effects [33], various chemicals isolated from herbal sources can be used in this therapy due to having fewer side effects. Extracts of gum ghatti *Anogeissus latifolia* [34], *Mangifera indica*, grape seeds [35], citrus peel [36] have been assessed to have hypo cholesterol activity and have been used traditionally for cholesterol-lowering activity.

Gururaja *et al.* [37] have shown that the methanolic extract of *Mangifera indica* leaf has significant cholesterol-lowering activity. Phytoconstituents like Iriflophenone 3-C-β-D glucoside, Mangiferin, β-taraxerol are quantified in Methanol extracts of mango leaves using High-Performance Liquid Chromatography [38] and are found to be 2.37% W/W, 4.6% W/W, 0.49% W/W respectively. The methanolic extract of the mango leaf has shown significant cholesterol-lowering activity in Albino Wister Rat. In this study, the dose 90 mg/kg is chosen to consider the human dose of 1.0 g/day. This single-dose study has shown a reduction of 14% serum cholesterol level compared to 17% and 63% reduction by atorvastatin, ezetimibe, respectively. In triglycerides, the reduction in triglycerides due to extract is 31% compared to 58% and 11% reduction caused by atorvastatin, ezetimibe, respectively. The non-toxic nature of the methanolic extract of *M. indica* is confirmed from the acute oral toxicity study as per Organisation for Economic Co-operation and Development (OECD) guidelines. The results indicated that the methanolic extract is non-toxic at the dose of 5000 mg/kg body weight of animals and test animals that have shown normal behaviour during 14 days.

Anti-proliferation and Pro-apoptotic Effect: Despite of the presence of various anti-inflammatory drugs available in the market, there is an ongoing search for new ones, especially those which are suitable for the treatment of chronic diseases, e.g., withinside the remedy of rheumatoid arthritis (RA). The main motto for this search is the reduction of adverse effects of the current drugs on one side, and more exact targeting of the cells on the other. Rheumatoid arthritis is a chronic, systemic, inflammatory disease that damages multiple joints in millions of patients worldwide. This disease is currently treated with steroids, non-steroidal anti-inflammatory drugs (NSAIDs), disease-modifying anti-rheumatoid drugs and ultimately with biological treatment mostly targeting the proinflammatory cytokines that are known to be involved in disease pathogenesis [39]. Each drug group mentioned is not fully successful and has various side effects; apart from these drugs have another problem which is its heavy economic impact. Therefore new, more efficient and better-targeted anti-Rheumatoid Arthritis agents should be invented. In this regard, much attention is paid to plant products, which are considered safe alternatives for synthetic drugs [40, 41].

Using advanced analysis of microscopic images and flow cytometry, it is demonstrated by Hene *et al*. [42] that naturally occurring xanthone and benzophenone derivatives have strong, dose- and O2 concentration-dependent anti-proliferative and pro-apoptotic effects on fibroblast-like synoviocytes (FLS) and macrophages of RA patients. Suspensions containing fibroblasts, macrophages and other infiltrating cells were obtained from inflamed synovial tissue collected from female RA patients. Cells growth was done in the presence of xanthone (mangiferin, isomangiferin, neomangiferin, norathyriol) or benzophenone (iriflophenone 3-C-glucoside, maclurin) derivatives within a time period of 48 h or 7 days, at 5% or 21% O_2.

Proportions of macrophages, FLS and infiltrating T cells undergoing apoptosis (Indicated by positive results of Annexin and 7-AAD), were determined by flow cytometry. The extent of late apoptosis

(DNA degradation) was assessed by fluorescent microscopy and image analysis in cultures where DNA was stained with Hoechst 33342. Most tested Benzophenone and Xanthone compounds exert anti-proliferative and pro-apoptotic, effects that were O2-dependent on T cells, FLS, and macrophages. The results indicate that xanthone- and benzophenone-rich plant products can be a basis for developing a dietary strategy for treating rheumatoid arthritis.

DISCUSSION: Iriflophenone 3-C-β-D glucoside is a very much valuable herbal constituent. It has many activities mentioned in this study, like antibacterial, antidiabetic, anti-inflammatory, cholesterol lowering, antioxidant, anti-proliferative and pro-apoptotic activity. As a antibacterial agent it has antibacterial potential against five bacterial strain and Iriflophenone 3-C-β-D glucoside has shown a strong antibacterial potential against *Klebsiella pneumoniae, Staphylococcus* aureus, and *Escherichia coli*, respectively. On the other hand, the least antibacterial potential is shown by Iriflophenone 3-C-β-D glucoside against *Bacillus subtilis*, in comparison to Cefixime. The cytotoxicity of Iriflophenone 3-C-β-D glucoside is significantly low against *Artemia salina nauplii*. As an antidiabetic agent, it lowers fasting and post prandial blood glucose levels.

The anti-inflammatory activities of this compound are revealed as the aqueous extract expressed strong IL-1α and IL-8 inhibitions, while the 70% ethanolic extract showed IL-1α and NO inhibition. It also has various activities like antioxidant activity, which is proved when Iriflophenone 3-C-β-D glucoside scavenged ABTS and peroxyl radicals ($TEAC_{ABTS}$ of 1.04 and $TEAC_{ORAC}$ of 3.61). Antihyperlipidemic activity is shown in methanolic extract of *Mangifera indica* leaf (where Iriflophenone 3-C-β- D glucoside is present) through the reduction of 14% serum cholesterol level compared to 17% and 63% reduction by atorvastatin, ezetimibe respectively. In triglycerides, the reduction in triglycerides is 31% compared to 58% and 11% reduction caused by atorvastatin, ezetimibe, respectively. It has anti-proliferative activity also as it exerts strong, dose- and O2 concentration-dependent anti-proliferative and pro-apoptotic effects on RA patients' fibroblast-like synoviocytes (FLS) and macrophages. Suspensions containing fibroblasts, macrophages and other infiltrating cells that were obtained from inflamed synovial tissue collected from female RA patients. There are various activities that are under research and yet to be discovered. As it has anti-proliferation activity, it can be used to treat various malignant tumours. These lots of effects make it a highly valuable compound. Conversely, this compound has very much fewer side effects as it is a herbal constituent. In that way, it can be a good alternative of any synthetic drug. This study intends to open a new window on the study of pharmacological effects of herbal constituents and formulation development as a whole in pharmacies in recent days.

ACKNOWLEDGEMENT: We would like to take the opportunity to express our special gratitude to our Director, Prof (Dr.) Abhijit Sengupta and Principal Prof (Dr.) Lopamudra Datta, for providing us the opportunity to work on this review. We would also like to thank our mentor Ms. Anuranjita Kundu for giving us his expertise and encouragement throughout this review's preparation. This review will help us to enlarge our knowledge and will also help us to improve our research skills. We also sincerely thank theJournal administrators for considering our review article.

CONFLICTS OF INTEREST: There is no conflict of interest between the authors of this review article.

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How to cite this article:
Bhattacharyya D, Nag S and Kundu A: The pharmacological actions of iriflophenone-3-C-B-D glucoside: an overview. Int J Pharm Sci & Res 2023; 14(9): 4384-92. doi: 10.13040/IJPSR.0975-8232.14(9).4384-92.