An Extensive Examination of Rice Bran's Anti-Diabetic Characteristics Additionally, This Might be Given Antioxidant Properties

Shiva Mishra[1*], Nayyar Parvez[1], Dr. Pranay Wal[2]

1. School of Pharmacy ,Sharda University , Greater Noida ,India
2. Pranveer Singh Institute of technology (Pharmacy) NH 19 Bhaunti Kanpur ,India

Correcponding author: **Shiva Mishra**

Abstract

Rice bran is one of the agricultural wastes that is rich in nutrients (RB). It features a wide range of minerals, lipids, proteins, fibers, trace elements, and minerals such as calcium, magnesium, manganese, potassium, and phosphorus. In rice bran oil, tocopherols, tocotrienols, oryzanol, and unsaturated fatty acids are prevalent. The separation and purification process has an impact on the quantity and quality of rice bran oil. Researchers have discovered that the bioactive components of RB have pro-, hypocholesterolemic, anti-inflammatory, anti-cancer, and anti-colitis properties. *In vitro and in vivo studies with human volunteers revealed that RB-derived substances were hypoglycemic-preventing agents.* A thorough update of the antidiabetic activity of RB and its derivatives is required to determine the state of the art in the relevant industry. The biological activity and composition of RB were examined in the current study, as were the effects of various solvent extraction methods on the biological properties of rice bran oil and rice bran extract. The current review focuses on the observed anti-hyperglycemia effects of rice bran derivatives as well as the most likely mechanism.

Keywords: Oryzanol, rice bran, rice bran oil, and anthocyanins, and anti-diabetic

Introduction

The complex metabolic condition known as diabetes mellitus is characterised by hyperglycemia (high blood sugar levels) brought on by deficits in insulin production, action, or both (DM). Insulin production is reduces and insulin resistance is supported by diabetes mellitus (DM), which is led on by damage to the pancreatic cells. Both type 1 and type 2 diabetes mellitus (DM) be accompanied by abnormalities of the pancreatic islet cells (defects in insulin secretion)[1]. And over 60% of the world's diabetics reside in Asia[2]. China and India are the best two countries with the largest proportion of adult diabetes, respectively. In 2015, were there 415 million cases of diabetes world. By 2040, that number should soar as many as 642 million[3]. Obesity, having an unhealthy lifestyle, not exercising enough, smoking, depression, and other inherited and aging-related variables, in particular, can cause type 2 diabetes[4]. DM has an effect on a person's lifespan in terms of health and socioeconomic development [4],[5]. About 10% of the total health care spending in affluent countries is spent on treating diabetes and its consequences [4]. Economic progress and a healthy way of life are threatened by the rise of DM frequency.

The bulk of people on earth consume rice as their main source of food, making it a useful cereal crop. Every year, well over 114 farmers grow 645 million tonnes of rice[6]. In 2050, rice production will be 12%–14% lower than it was in 2000, according to a model created by the International Food Policy Research Institute. Climate change will have an impact on rice growth

globally. It was also forecast so a loss of around 65 million tonnes would noticeably impact the value of rice in South Asian countries, which would decrease consumption rates, raise costs, and impair child malnutrition.[7]. Many byproducts are generated during milling of rice, namely rice's bran and husk (the outer layer of the rice kernel is composed of the pericarp, aleurone, sub-aleurone layer, and germ). animal grub [6] The meals made by milling rice are used to produce a range of items, including bedding material. Rice bran (RB) (tocopherols and tocotrienols) is a major source of these compounds[8].

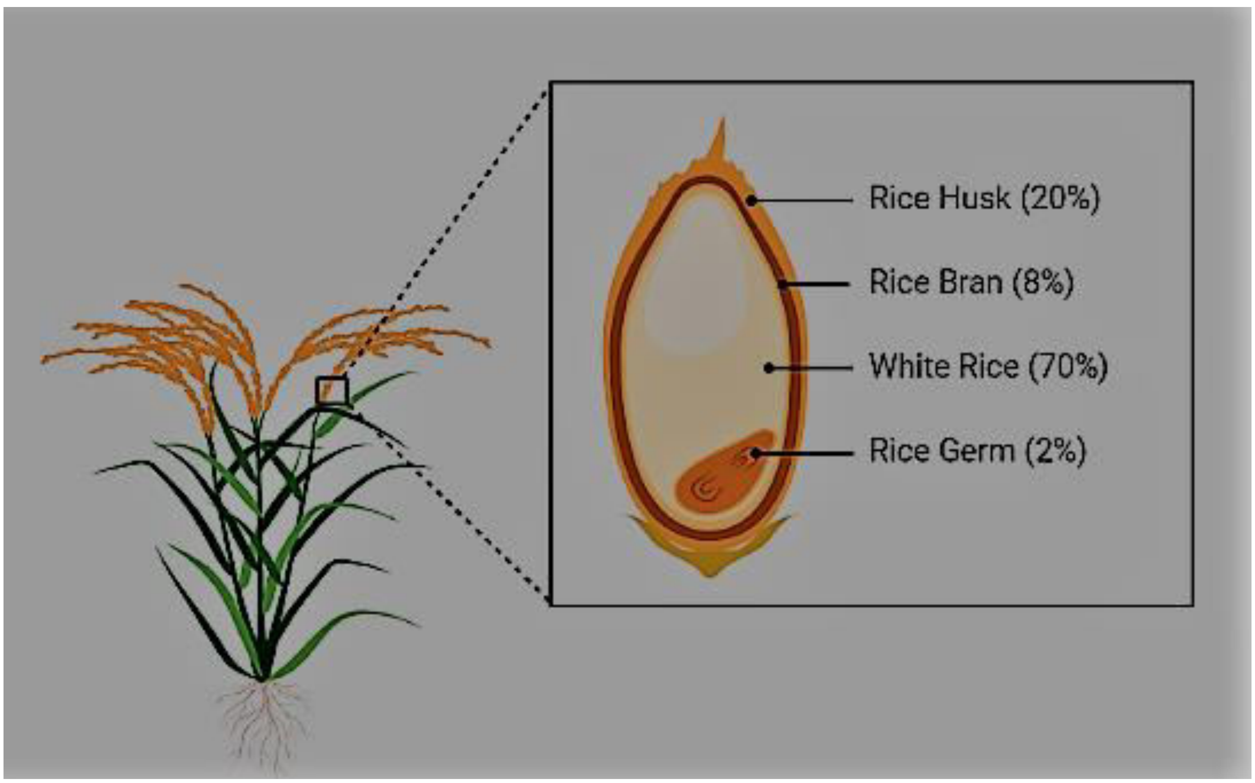

Figure 1 Plant of Rice Bran

Rice bran contains oil, sometimes referred to as rice bran oil, in amounts of 15% to 20% (RBO). The health benefits of RBO are widely documented[8]. The RBO's amount and quality varied according on the cultivars, the extraction process, and other elements[9],[10]. We are using and developing brand-new, environmentally friendly, solvent-free extraction procedures to obtain better grade RBO from RB. Due to its strong nutraceutical value and rich fatty acid makeup, RBO is used in both the food and pharmaceutical sectors. One of the most popular cooking oils in Asia, particularly in Thailand, South Korea, China, Taiwan, and Japan[11].

Numerous health benefits of RBO have been found. The current study combines RBO's known anti-diabetic capabilities with an overview of its composition, bioactivities, and the effects of the extraction process on RBO's quality.

2. Rice bran's makeup and health advantages

RB includes a variety of minerals and other elements, notably manganese, magnesium, calcium, phosphorus, and potassium. Lipids (15%–20%), proteins (11%–15%), fibres (7%–11%), and carbohydrates (34%–62%) are also included[12],[13]. According to RBO, fatty acids can be either

saturated or unsaturated in varying amounts. The composition consists of 38.4% oleic acid, 34.4% linoleic acid, 21.5% palmitic acid, 2.9% stearic acid, 2.2% linolenic acid, and other acids. [14]. The beneficial components in RBO are shielded from oxidative deterioration due to the high levels of

tocopherols, tocotrienols, and oryzanol[14],[15]. The majority of RB is composed of defatted crude fibre (1.8%), reducing sugars (12.44%), protein (14.27%), ash (14.59%), and carbs (58.41%) [16].

The RB extracts contain a number of phenolic and anthocyanin-containing compounds. The anthocyanin concentration varied amongst cultivars in both of richness and variety. Rice varieties that colour include a lot of phytopigments. The phytochemical content of Thai rice varieties (black, brown, and red rice varieties) varied, with total phenolic content ranging from 36.14 to 0.36 to 0.00 to 487.25 mg of cyanidin per gramme of extract, that equivalent 1.93 mg of quercetin and 305.30 mg of gallic acid equivalent per gramme of extract, respectively[17]. Non-polar extraction of RBO generated RBO with a different quality in terms of total tocols and oryzanol content, much like polar extraction provides [10].

The fact that RB is a valuable food item since it is a rich source of proteins and is hypoallergenic and essential amino acids [18],[19]. RB is the major nutritional source. fibres since they have a laxative effect, which helps to increase faecal output[20]. Consuming 10 grammes of dietary fibre daily, whether from fruit, cereal, vegetables, or all three sources combined (total dietary fibre), decreased the odds of dying from coronary heart disease by 30%, 25%, 0%, and 27%, respectively[21]. Because of this, fruits and grains are excellent sources of fibre that lower the chance of severe coronary heart disease. One of the many bioactivities that have been noted is the potential of rice unsaponifiables, especially oryzanol, to lower cholesterol and low-density lipoprotein levels[22],[23],[24].Some properties of certain rice phytochemicals include trypsin and pepsin inhibition as well as anti-thiamine activities[25].

Strong antioxidants found in RB[26, 27] can help cure and control oxidative stress-related illnesses, cancer[29,30], colitis brought on by dextran sodium sulphate in vivo[32], and other diseases. The antioxidant, anti-cancer, and cholesterol-lowering effects of rice tocotrienols have been noted[33, 34, 35]. By treating hyperlipidemia, lowering plasma cholesterol, reducing platelet aggregation, reducing cholesterol absorption, and reducing the symptoms of menopause, the RB became a potential source for nutraceuticals because to its high content of oryzanol[36]. Furthermore, apoptosis induction, aldose reductase inhibition, and a decrease in cancer cell invasion have all been associated with rice anthocyanins[37, 38, 39].

1. **Impact of extraction methods**

The extraction procedure alters the phytochemical content of the RBO (contains oryzanol and tocols) and RB extracts (contains phenolic compounds, flavonoids, and anthocyanins). The bioactive components of RB are recovered using solvent extraction methods (ethyl acetate, isopropanol, heptane, ethanol, and methanol), cold pressing, hot pressing, supercritical fluid extraction (SFe), microwave, and ultrasonic-assisted extraction techniques used Imsanguan et al.'s [40] evaluation of three distinct extraction techniques, including solvent, supercritical CO2, and soxhlet extraction, on the production of oryzanol and tocopherol from RB. The research demonstrated that compared to hexane-based soxhlet extraction, supercritical CO2 extraction produced a high yield of tocopherol more quickly (and in a shorter amount of time). RB was able to extract significant yields of oryzanol using supercritical CO2 as well [40]. According to the cultivars, the quantity and quality of the extract varies. In some Thai rice bran, Pengkumsri et al.[10] examined the impact of different extract on the production of oryzanol and tocols containing RBO as well as the antioxidant capacity of RBO. Hexane extraction showed a high yield when compared to SFe, cold press, and hot press techniques. Different cultivars also produced a variety of yields. In terms of the total number of protocols and free radical scavenging activities, the research revealed the solvent extraction was better than SFe and pressing techniques[10]. Azrina et al. gave a detailed description of the use of solvents for the extraction of oryzanol and the total lipid content of RB.

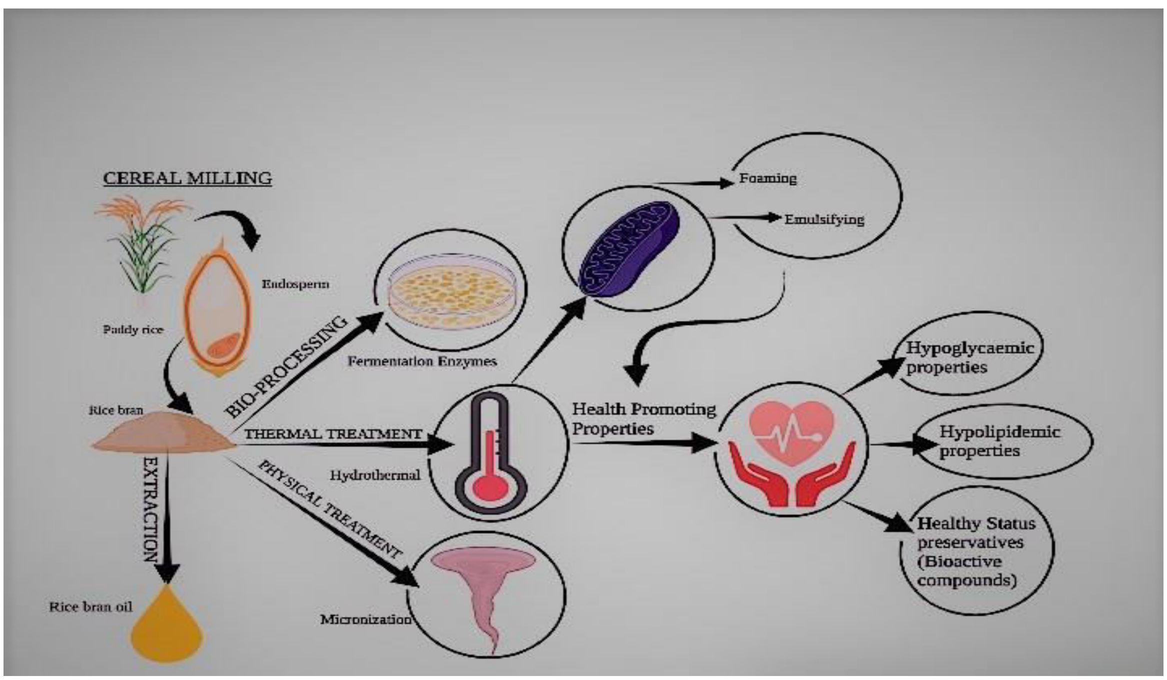

Figure 2. Rice bran extraction for hypoglycaemic properties

It's likely that the solvents used to remove RB from the completed product left some solvent residue behind. Solvents shouldn't be present in RBO and RB extracts utilized in the food and pharmaceutical sectors. To securely extract the RBO without using solvents, SFe methods [43], heat and cold pressing [42], and both are used. The RBO yield % of the SFe process is affected by temperature and pressure [44]. The mixed solvent extraction approach produced half as much

oryzanol from RB as the SFe method did [45]. In both the solvent extraction and SFe procedures, the RBO quality and quantity are affected by the temperature, pressure, and extraction time.

When compared to traditional solvent extraction techniques in terms of a number of attributes, iodine content, wax, and the makeup of the fatty acids, Terigar et al.'s [46] findings indicated that continuous microwave-assisted extraction produced excellent quality RBO. In terms of higher recovery of total phenolic contents and better antioxidant activity, microwave RB preparation before SFe provided superior quality extract [47]. High yields of RBO with increased bioactivity were produced when ultrasonic pre-treatment and conventional extraction were combined [48],[49] .High yield, repeatability, reduced time and solvent consumption, low temperature, and environmental friendliness are a few advantages of ultrasonic-assisted extraction over conventional extraction techniques [50].

It's essential to achieve the best results to keep the ideal conditions, such temperature and treatment time, in place. High-quality RBO and RB extracts are still used in the food and pharmaceutical industries for a variety of uses[51] despite the fact that heat and microwaves harm anthocyanins, one of the main bioactive components of RB extract.

2. Rice bran has anti-diabetic properties

4.1. ***Clinical Studies***

According to research, the stabilised RB, RB water solubles, and RB fibre concentrates are excellent nutraceuticals for alleviating diabetes-related problems in people. After receiving these RB fractions [6 groups received stabilised RB, RB water solubles, and RB fibre concentrates in 6 different sequences; Each product was administered for 8 weeks with a washout period (4 weeks) between the administration of each product; Dosage: 20 g per day], both type 1 and type 2 diabetic patients demonstrated a significant reduction in blood sugar levels their serum insulin levels improved. Moreover, some who took RB fibre concentrates had smaller levels of LDL cholesterol, total blood cholesterol, triglycerides, and apolipoprotein B[52]. Individuals with type 1 and type 2 diabetes had reduced fasting and postprandial blood glucose levels when they supplemented their diets with a low-fiber diet for one week, then a diet high in fibre for the following week (40 g of rice bran fibre daily). A high-fiber diet was also demonstrated to increase faecal weight [53] and to in stool samples that include lactose. While postprandial glucose, HbA1c, total cholesterol, and LDL cholesterol levels decreased in people with type 2 diabetes who took RB (20 g per day for around 12 weeks), adiponectin levels have risen[54] . While RBO-modified milk (18 g RBO per day for five weeks) improved LDL cholesterol and total blood cholesterol levels, it did not reduce insulin resistance in type 2 diabetes [55]. According to Shakib et al. [56], RBO (30 g per day) used in salad dressing and cooking for six months, and this led to decreased levels of lipids, insulin, and triglyceride. HbA1C, fasting and postprandial blood sugar, liver transaminases, blood urea, erythrocyte sedimentation rate, serum uric acid, and other parameters are followed in type 2 diabetes patients. To the author, adding RBO to a healthy diet may lower your risk of cardiovascular disease.

Patients with type 2 diabetes who administered an oil mixture (20% sesame oil and 80% RBO) at fasting and postprandial periods for eight weeks saw benefits in the levels of high-density cholesterol, low-density lipoprotein cholesterol, total cholesterol, and triglyceride [57]. According to a comparison study on the therapeutic value of these three types of oil in individuals who have type 2 diabetes, RBO and canola oil may be beneficial for diabetic patients (postmenopausal women). RBO and canola oil, in its respective ratios, vastly reduced triglycerides, LDL cholesterol, and total blood cholesterol[58].

*4.2. **In vivo research***

RB extract (0.1% Ricetrienol®) had a protective decrease plasma MDA and increasing plasma tocopherol and glutathione peroxidase 1 transcription in the obese, diabetic KKAy mice. While Ricetrienol® (0.1%) was effective in curing hyperlipidemia and hyperglycemia, it was found to be helpful in avoiding the effects of oxidative stress [59]. In streptozotocin-induced diabetic (DM) rats, RBO treatment diminished oxidative damage [60] Hsieh and additional [60] This research showed how a four-week RBO intervention decreased dramatically the quantity of 8-hydroxy-2'-deoxyguanosine, a recognised molecule to assess the oxidative DNA damages, in mitochondrial DNA. According to Chen and Cheng [61], the RBO's high concentrations of tocotrienol and oryzanol may be the reason of its antidiabetic effects. RBO In streptozotocin/nicotinamide-induced type 2 DM mice, a diet high in tocotrienol and oryzanol (10 g or 15 g per 100 g of chow for four weeks) lowered plasma triglyceride, hepatic triglyceride, and plasma LDL cholesterol levels. Along with the excretion of neutral sterol and bile acid from the faeces reductase is the thing, RBO administration also raised the mRNA levels of the 3-hydroxy-3-methylglutaryl coenzyme, LDL receptor, and 7-hydroxylase in the hepatic[61] .

The anti-hyperglycemic effect of the tocotrienol-rich fraction was investigated[62] using type 1 DM-induced male Wistar rats and streptozotocin (55 mg/kg body weight) (extracted from palm oil and RBO). Treatment for eight weeks with a In type 1 DM rats, Fasting blood sugar, HbA1c, and serum nitric oxide levels were all reduced by a tocotrienol-rich portion of RBO (200 mg/kg body weight per day). Additionally, treating an experimental DM animal with a tocotrienol-rich fraction of RBO reduced urine nitric oxide levels and increased levels of antioxidant enzymes, respectively, to avoid nitrosative and oxidative damage to kidney tissues[62]. In type 2 DM rats, RBO generated by streptozotocin and nicotinamide has been shown by Chou et al. [63] to have protective benefits. RBO supplementation enhanced HDL cholesterol, for five weeks, type 2 DM rats' excretion of bile acids and neutral sterols decreased hepatic cholesterol, the atherogenic index, and the hyperinsulinemic response (150 g RBO per kg diet). The phenolic acid caused C57BL/KsJ db/db mice component of RB (17 days of intervention) may promote hepatic glucokinase activity and reduce blood sugar levels.

By raising the amount of antioxidant enzymes, oryzanol (50–100 mg/kg body weight) treatment for 11 days improved the liver's antioxidant capacity in streptozotocin-induced diabetes mellitus rats. In diabetic rats treated with oryzanol, blood glucose levels reduced and lipid peroxidation was reduced in a dose-dependent manner [65]. The health of streptozotocin-induced diabetic rats was

improved by additional Thai purple sticky rice bran (50 g/kg; 8 weeks) by increasing insulin sensitivity and decreasing plasma glucose, free fatty acid, and triglyceride levels[66].

Thai rice bran oil with colour (5.0, 7.5, or 15% of RBO) also was given to streptozotocin-induced diabetic rats

who were fed a high-fat diet for 12 weeks. As a result, serum MDA levels drop, while levels of catalase, coenzyme Q10, glutathione peroxidase, superoxide dismutase, and oxygen radical absorption capacity all increased. After being fed a high-fat diet, rats receiving RBO therapy had their damaged pancreas, kidney, heart, and kidneys returned to their pre-damaged state [67]. The hepatic enzyme which regulates glucose uptake is regulated, one of the main mechanisms driving RBO's anti-diabetic benefits. Glucokinase activity was increased in RBO-supplemented C57BL/6N mice (30% RBO for seven weeks) fed a high-fat diet, whilst phosphoenolpyruvate carboxykinase activity was lowered and glucose-6-phosphatase activity has been increased[68]. According to[69], in C57BL/6J mice fed a high-fat diet, oryzanol (20 or 80 g/g body weight; 13 weeks intervention) and brown rice (30% of the Chow diet) enhanced glucose metabolism and reduced hypothalamic endoplasmic reticulum stress. Oryzanol alters blood glucose levels, the probability of hyperglycemia, and the function of hepatic glucose-regulating enzymes [70],[71]. Oryzanol[72] controls the release of adiponectin by preventing NF-B from activating.
The anti-diabetic effects of the ethanolic extract of black rice bran were reported in Sprague Dawley rats that were given 150 mg/kg of alloxan [73]. Ethanolic RB extract therapy (100 or 200 mg/kg body weight) for four weeks shown a strong ability to reduce blood sugar and high levels of insulin by regenerating pancreatic beta cells in diabetic rats [73].

*4.3. **In vitro research***

A black rice bran ethanol extract inhibited glucosidase with an IC50 of 121 mg [73]. An in vitro analysis revealed that RB extracts reduced the activities of the enzymes glucosidase and amylase while accelerating the glucose digestion by 3T3-L1 adipocytes. The findings of the molecular regulation investigation showed the RB extract enhanced the mRNA expression of the glucose transporters GLUT1 and GLUT4, as well as IRS1 and IRS2 [74]. As they examined the anti-diabetic properties of the Egyptian-stabilized RB extract, they reported that the extract's ability to stimulate the release of insulin from INS-1 cells was dose-dependent [75].

3. Conclusion and potential outcomes

RB is well known for its abilities to improve health and is an abundant source of vital nutrients. Tocols, dilatory fibres, oryzanol, and other significant fatty acids are thought to be responsible for the bioactivities of RB. According to research, adding RBO, RBE, and oryzanol fraction to one's diet significantly reduced hyperglycemia and the consequences it had by regulating the activity of hepatic enzymes that regulate glucose metabolism and the proteins that comprise the insulin signalling. However, the therapeutic benefits of RB were not fully used. It is essential to do a proper examination of the dosage, duration of therapy, and other important nutraceutical operations. The development of functional meals based on RB and increased public knowledge of the use of Fullback products in daily life may assist industrialised and developing nations manage hyperglycemia adequately.

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Abbreviation IC_{50}-Half maximal inhibitory concentration
INS-1-Insuline protein coding gene
INSR-Insuline Receptor
KKAy-mice are cross between diabetic & lethal yellow
LDL-Low density lipid
MDA-Malondialdehyde
mRNA- Messenger ribonucleic acid
NF-κB- Nuclear factor kappa B
RBE-Relative biological Effectiveness
RBO- Rice bran oil
RB-Rice bran
SFe-Supercritical Fluid Extraction
3T3-L1-Cell line derived from mouse
C57BL-Common inbred strain
CO_2-Carbon dioxide
DM-Diabetes mellitus
DNA-Deoxyribonucleic acid
GLUT 1- Glucose Transporter-1
GLUT 4- Glucose Transporter-4
HbA1C- Hemoglobin A1c
HDL-High density lipid

Graphical Representation-