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Antidiabetic Effect of Ginger (*Zingiber officinalis*) and Oregano (*Oregano vulgare*) in BPA Induced Catfishes

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Abstract: ***BPA is a widely used compound in daily life. Therefore, there are various routes of human exposure to this substance such as oral, by inhalation and transdermal. BPA has been shown to play a role in the pathogenesis of several endocrine disorders including female and male infertility, diabetes. The purpose of this study is to review the available knowledge of epidemiologic evidence on BPA exposure and diabetes and to know the value of alternative medicine to cure diabetes.***

Keywords: BPA, diabetes, Ginger, oregano

1. Introduction

Bisphenol A (BPA) belongs to chemicals that are produced in the large quantities. It is commonly used as a plasticizer and an intermediate in the synthesis of epoxy resins, polycarbonate plastics [1] as well as an additive for the elimination of surfeit of hydrochloric acid during the polyvinyl chloride (PVC) fabrication. BPA is widely used in the production of healthcare equipment [2], dental composites [3], contact lenses, spectacle lenses, toys, storage media and window foils [4].

BPA is one of the Food Contact Materials (FCMs), which means that it is used in the preparation of plastics for the manufacture of materials that have direct contact with food [5], plastic packaging, kitchenware, jar cap coatings, and the wall of cans that isolates the food from metal, therefore preventing its corrosion [6].

Hence, BPA is a widely used compound in daily life. Therefore, there are various routes of human exposure to this substance such as oral, by inhalation and transdermal. BPA has been shown to play a role in the pathogenesis of several endocrine disorders including female and male infertility, **diabetes**, precocious puberty, hormone dependent tumours such as breast and prostate cancer and several metabolic disorders including polycystic ovary syndrome (PCOS) [7].

Diabetes mellitus is a chronic metabolic disease which now afflicts 10 % of the world population. It is considered a "modern-day epidemic" and is rightly recognized as a global public health issue [8]. The characteristic features of this disease include glucose intolerance, insulin resistance in skeletal muscle, adipocytes and liver, and often compensating hyperinsulinemia at the onset of this pathology. At later stages, b-cell function is affected leading to a decrease in insulin release and lower levels of plasma insulin, which favors hyperglycemia. Insulin resistance can develop in response to the environment and results from a complex interplay between nutrient overload, systemic excess of fatty acids, adipose tissue inflammation and oxidative stress [9].

Some spices which have been reported to exert hypoglycemic effect both in laboratory animals and human subjects are: Ginger (***Zingiber officinalis***), Fenugreek seeds (*Trigonellafoenumgraecum*), Oregano (***Oregano vulgare***).

Clariasgariepinus(Catfish) is widely distributed in Africa and parts of Asia (Israel, Syria and south of Turkey). Its main habitats are calm lakes, rivers and swamps in areas that flood on a seasonal basis [10&11]. *C. gariepinus*has pseudolungs, long bodies and a high capacity to produce mucous as adaptations to live in stagnant environments or out of water [12].

2. Materials and Methods

2.1. Plant Materials

- *Oregano vulgare* (Oregano) is an aromatic, woody-based perennial, which has been used as a folk medicine.

2.2. *Zingiber officinalis* (Ginger) is a flowering plant whose rhizome and ginger root is widely used as a folk medicine. It also has the ability to normalize blood glucose levels.

2.3. Preparation of Herbal Extract

2.2.1 Oregano vulgare

The leaves of Oregano were washed thoroughly in tap water, shade dried, and powdered.

Figure 1: Prepared Oregano Powder

2.2.2 Zingiber officinalis

Fresh ginger roots were soaked, washed thoroughly in tap water, dried, and powdered.

Figure 2: Prepared Ginger Powder

2.4. Experimental Animals

The catfishes about 400-450g was maintained at $24+1^0$ C with alternate 24hours light/dark periods and the animals were fed on a standard laboratory diet and water.

Figure 3: *Clariasgarienpinus* (Catfish)

2.5. Experimental Protocol

The fishes were divided into four groups comprising of two animals in each group.

Table 1: Experimental Protocol

Groups	Experiments
Group I	Control-sham operated animals (C)
Group II	BPA induced animals for 07 days as experimental control [BPA (EC)]
Group III	BPA induced animals after 07 days given herb extract 1 (*Oregano vulgare*) [T1 (HE)]
Group IV	BPA induced animals after 07 days given herb extract 2 (*Zingiber officinalis*) [T2 (HE)]

The study was carried out to assess the diabetes in the blood of BPA induced fishes and to find the efficacy of herbal extract supplementations.

2.6. Hyperglycemic activity

Hypoglycemic study was conducted to test the efficacy of the leaf extract as per the method described earlier in four different experimental model groups and the blood sugar lowering efficacy of the herbal extract was studied.

2.7. Oral Supplementation of BPA

Bisphenol A (BPA) (40mg/kg body weight) was mixed with drinking water and given directly to the fish containing water.

Bisphenol A

2.8. Herb Extract Supplementation 1

Fishes are fed with herb extract [*Origanum vulgare* (200mg/kg body weight)] which was mixed with drinking water.

2.9. Herb Extract Supplementation 2

Fishes are fed with herb extract [*Zingiberofficinale*(200mg/kg body weight)] which was mixed with drinking water.

2.10. Estimation Of Blood Glucose

In each case 200μl of blood sample was collected from behind the fin of lateral line of fish and estimated with the help of glucometer. The blood samples were collected from behind the fin of lateral line of fishes of four groups and estimated the glucose with the help of glucometer.

Figure 4: Glucometer Showing Blood Sugar Value of BPA Induced Catfish

3. Result

In this study, the level of blood glucose, insulin after using a 40 mg/kg dose of Bisphenol A, ensured induction of diabetes in catfishes. The blood- glucose levels rose markedly after BPA administration, and the high glucose levels were maintained for 7 days (Table 2). Oral administration of the *Zingiber officinalis* extracts (200mg/kg) and *Oregano vulgare* extracts (200mg/kg) produced a significant decrease in blood-glucose levels in BPA diabetic (Table 3&4). Treatment with folklore medicine, showed reduced blood-glucose levels as compared to control group.

Table 2: Effect of Bisphenol A

Control Fishes (C)	Experimental Control BPA (EC)
140 mg/dl	247mg/dl

Table 3: Effect of Oregano (*Oregano vulgare*) Extract on BPA Induced Catfishes

Control Catfishes (C)	Experimental Control BPA (EC)	Treated with Herbal Extract at 2nd day [T(HE)]	Treated With Herbal Extract at 4th day [T(HE)]	Treated With Herbal Extract at 7th day [T(HE)]
140mg/dl	247mg/dl	220mg/dl	181mg/dl	136mg/dl

Table 4: Effect of Ginger (*Zingiber officinalis*) Extract on BPA Induced Catfishes

Control Catfishes (C)	Experimental Control BPA (EC)	Treated with Herbal Extract at 2nd day [T(HE)]	Treated With Herbal Extract at 4th day [T(HE)]	Treated With Herbal Extract at 7th day [T(HE)]
140mg/dl	247mg/dl	218mg/dl	176mg/dl	129mg/dl

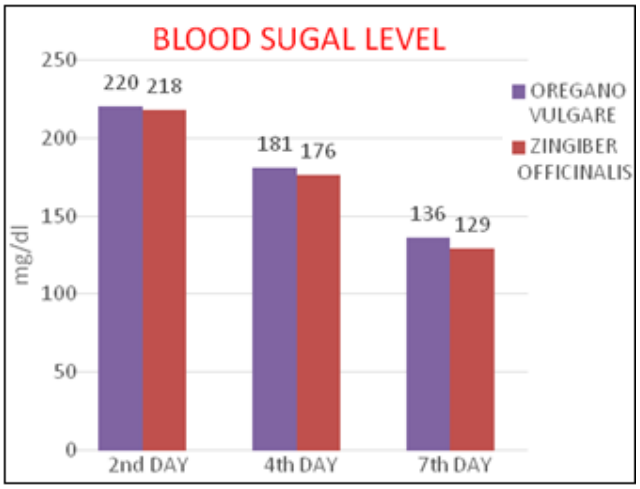

Figure 5: Graph Showing Blood Sugar level of Catfish in both Oregano and Ginger

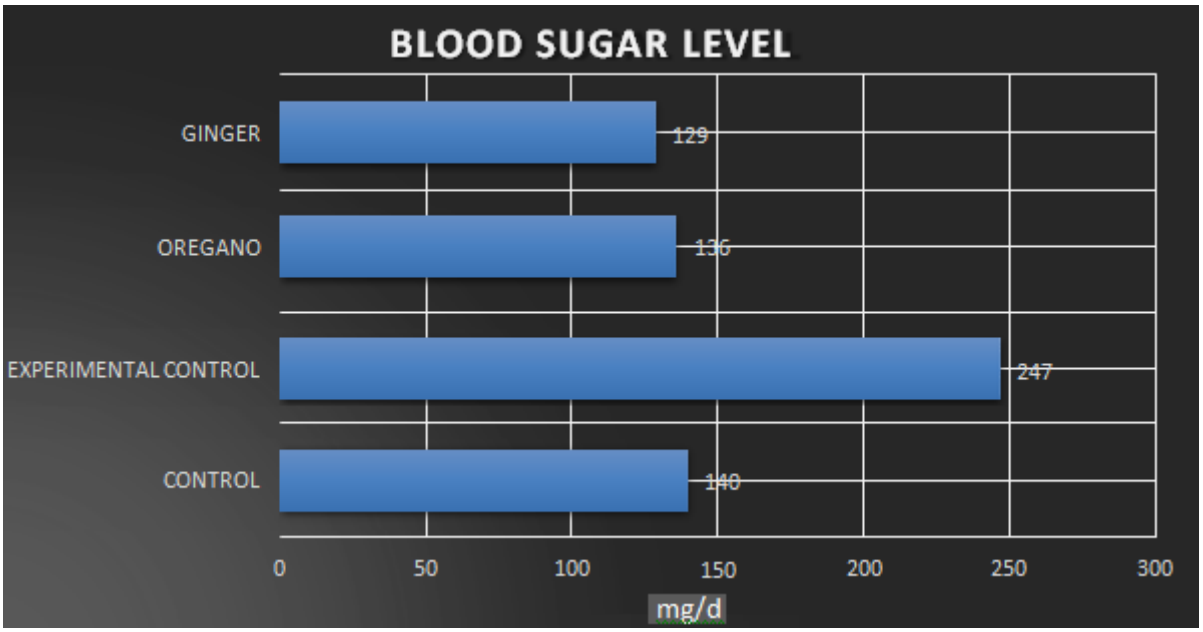

Figure 6: Graph Showing Blood Sugar Level of Catfish

4. Discussion

In the present study we demonstrate that exposure to low doses of BPA promotes adverse effects on glucose homeostasis and insulin action on peripheral tissues with the concomitant risk of developing diabetes. Fishes treated with BPA during 7 days presented no increase in weight and normal non-esterified fatty acids (NEFA) levels; however they presented insulin resistance and had a strong tendency to be hyperinsulinaemic in the fed state, together with decreased glucose levels. The hyperinsulinaemia in the fed state may be explained by an improved stimulus secretion coupling of b-cells, because islets isolated from BPA treated fish displayed a greater release of insulin in response to high glucose. The stimulatory action of BPA on islets may be due to an adaptation to the peripheral insulin resistance or to a direct action of BPA on b-cells or both. In any case, a direct action of BPA is very likely because it has been demonstrated in isolated islets from fish and fishes that low doses of BPA potentiates GSIS as well as pancreatic insulin content. Fluvestran blocks BPA action on GSIS pointing to an involvement of estrogen receptors.

In spite of the presence of known antidiabetic medicine in

the pharmaceutical market, herbal drugs are frequently considered to be less toxic and also free from side effects, than synthetic ones.

In the present study, the administration of BPA induced hyperglycaemia in fishes. Treatment of diabetic fishes with oregano at 200 mg/kg showed a significant decrease in the blood-sugar level. This may be due to that *Oregano vulgar* enhance the insulin sensitivity of the receptors on cells, leading to reduced levels of blood sugar and more energy production. The accumulating evidence suggests that modulation of insulin secretion and/or insulin action mechanisms could be involved in the antidiabetic effect of oregano. This evidence was confirmed with Talpur*et al*. (2005) who reported that extracts of oregano improve blood sugar levels by enhancing insulin sensitivity.

Zingiberofficinale(Ginger) shows effective glycaemic control properties in diabetes mellitus. The mechanisms underlying these actions are associated with the inhibition of key enzymes controlling carbohydrate metabolism and increased insulin release/sensitivity, resulting in enhanced glucose uptake in peripheral adipose and skeletal muscle tissues. The prominent lipid lowering effects of ginger also contribute to improving the insulin resistant condition. A protective effect of ginger against diabetic complications is also an important aspect of its benefits. Pharmacokinetic and bioavailability studies provide further information for understanding the metabolism of ginger, especially its pungent principles. Sufficient acute and chronic toxicity studies have demonstrated the broad safety of ginger as a complementary hyperglycaemic control agent.

5. Conclusion

The present investigation clearly showed that the herb extracts of Ginger and Oregano had a very great potential as drug alternative in diabetic patients and related disorder demonstrated significant antidiabetic activity. In conclusion, our present study reveals that the herb extracts of Ginger and Oregano had potential effects in improving blood sugar level in BPA induced diabetic catfishes. This study provides experimental evidence that two herb extracts may be a potential therapeutic agent for hyperglycemia that is associated with diabetic complications.

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