Investigation of the role of curcumin against the toxicity induced by bisphenol a on the reproductive system in male rats

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Abstract

Bisphenol A (BPA) is an endocrine disruptor and an environmental pollutant; it can produce free radicals, which cause damage in various tissues. Curcumin has been demonstrated to help with a variety of male reproductive diseases, as well as to scavenge free radicals and function as an antioxidant. The aim is to estimate the protective role of Curcumin against the toxic effect of BPA in male rats by determining the levels of antioxidants and sexual hormones, before and after treatment with this herb. The effect of curcumin as a protective role against BPA on the oxidative stress parameters showed that Curcumin could decrease MDA concentration and at the same time increase the concentration of both catalase and SOD. Also, the results revealed that Curcumin could increase the concentration of LH, FSH, and testosterone as compared to the BPA-treated group .

Keywords: Bisphenol A (BPA), Reproductive hormones, Curcumin, Antioxidants, Herbs

Introduction

Bisphenol A (BPA) is a widely produced chemical that is commonly found in various consumer products, including epoxy resins, polycarbonate plastics, food packaging, dental sealants, PVC, and thermal paper receipts. As a result, both humans and animals can be exposed to this chemical through different routes, such as ingestion, inhalation, and skin contact [1]. BPA, or bisphenol A, is classified as both an environmental pollutant and an endocrine disruptor. It has the ability to generate free radicals and cause damage to tissues [2]. In addition, BPA has been recognized as an estrogen-mimicking disruptor and is extensively employed in several industries. Water pipes, computer equipment, paper, and toys are among the myriad of everyday items that incorporate it. Bisphenol A (BPA) can leach from polycarbonate plastics, particularly when they are exposed to heat. It has been observed that BPA, when released from plastics, attaches to the estrogen receptor ; Nevertheless, certain studies indicate that

BPA can potentially exert detrimental effects on the reproductive system, central neurological system, and immune system [3]. The physiology of the reproductive system involves intricate biological processes that can be influenced by exposure to environmental contaminants. This exposure may partly contribute to the rise in pathologies within the male reproductive system, specifically known as testicular dysgenesis syndromes. These syndromes encompass conditions such as cryptorchidism, hypospadias, reduced sperm production, and testicular cancer [4]. Bisphenol A (BPA) has the ability to interact with and bind to androgen receptors, which can negatively impact reproductive function. This can lead to diminished male fertility, including conditions such as cryptorchidism, testicular dysgenesis, and cancer [5]. Animal studies have demonstrated that it also negatively affects sperm quality and disrupts the integration of germ cell nests [6].

In addition, estrogen receptors are distributed across various organs including the thyroid glands, reproductive organs, and other organs. Consequently, the interaction between BPA and these receptors results in heightened cellular expression, thereby impacting sexual maturity [7]. Plants contribute approximately thirty percent of all current medications and have a rich historical association with fertility-related folklore, including their aphrodisiacal and fertility-enhancing properties. Plants and substances derived from plants have been recognized for their biological properties and have been important in global healthcare [8]. Curcumin, with the scientific name "Curcuma longa," chemical name "diferuloylmethane," and molecular formula C21H20O6, is an important compound found in the turmeric plant [9]. Moreover, experimental studies have demonstrated that curcumin effectively addresses several male reproductive problems, hence enhancing fertility [10]. The positive benefits of curcumin may be attributed to its capacity to scavenge free radicals and function as an antioxidant agent, as well as its ability to elevate serum testosterone levels [11].

Materials and Methods

Experimental Design :

Thirty adult male rats were utilized in this study conducted at the College of Veterinary Medicine at the University of Kerbala. Their mean weight fell within the range of 200 to 350 grams, while their ages spanned from 14 to 16 weeks. After 15 days of being confined in metal cages with controlled climatic conditions (maintained at 23±2 °C and a 12-hour light-dark cycle) and provided with daily access to water and food, the animals were randomly assigned to four groups, each consisting of six individuals.

1 -Group 1(Control Negative Group): Animals received orally normal saline, daily for 5 weeks.

2 -Group 2 (BPA): received Bisphenol A (100 mg/kg) of body weight daily, oral gavage for 5 weeks

3 -Group 3 (BPA+ Curcumin): Animals received BPA (100 mg/kg) + Curcumin 100 mg/kg, orally gavage daily for 5 weeks.

4 -Group 4(Curcumin): Animals received Curcumin 100 mg/kg, orally gavage daily for 5 weeks. This group used as a positive control group to confirmed that, there was no toxic effect of Curcumin and the toxic effect (if present) belonged to BPA solely .

BPA (purification more than 97 %) was obtained from high media company (India), Curcumin herb obtained from local market and it was confirmed by specialist in botany .

Parameters Studied: After the end of the experiment blood serum was taken for the laboratory tests, according to the following :

-Physiological parameters

1-Measuring the level of (Superoxide dismutase , catalase (CAT) and Malondialdehyde (MDA) by using ELISA and the specific kits provided by (Sunlog/China).

2 -Sexual Hormones (Luteinizing hormone (LH), Testosterone and Follicle-stimulating hormone (FSH)). Using ELISA and the specific kits provided by (Sunlog/China). Using ELISA and the specific kits provided by (Sunlog/China).

Statistical Analysis: Using the t-test and a significance threshold of $P \leq 0.05$, the statistical tool Graph Pad Prism 8.0 was utilized. The information was displayed as mean ± SD.

Ethical Approval: The study was conducted in adherence to the ethical principles outlined in the Helsinki Declaration. The study protocol, subject information, and permission form were examined and authorized by the local ethics committee under the reference number UOK. VET. PH.2023.082.

Results and Discussion

In this study the protective role of Curcumin investigated to eliminate the toxic effect of BPA against reproductive system .

As mentioned above, the last group used to detect that, the curcumin had no toxic effect and the toxic effect if present was due to BPA only. Therefore, the effect of curcumin estimated on oxidative stress parameters (MDA, superoxide dismutase and catalase), hormones of reproductive system (FSH, LH and testosterone). The results obtained, showed in the table (1).

Table (1): The effect of curcumin on the oxidative stress parameters and reproductive hormones

Parameter	Mean of control	Mean of Curcumin	*P* value	Significant?
MDA (µl)	16.12	20.10	0.6770	NO
SOD (U/ml)	260.2	261.1	0.7587	NO
Catalase (µl)	6.510	7.437	0.7398	NO
FSH (ng/ml)	28.19	26.15	0.3965	NO
LH (IU/L)	4.214	5.136	0.6306	NO
Testosterone (pg/ml)	246.9	250.1		NO

P value< 0.05 significant

The results confirmed that, there were no significant values between the control group and Curcumin group to exclude the effect of Curcumin according to parameters used in this study .

The effect of curcumin as a protective role against BPA on the oxidative stress parameters, showed that Curcumin could decrease MDA concentration and in the same time increase the concentration of both catalase and superoxide dismutase (Table 2) .

Table (2): The effect of curcumin vs. Bisphenol A on the oxidative stress parameters MDA, SOD and catalase

Parameters	Mean of control	Mean of BPA	Mean of BPA+Curcumin
MDA	**16.12**	**36.88**	**17.83**
SOD	**261.1**	**28.44**	**169.2**
Catalase	**6.510**	**1.424**	**7.994**
***P* value**	**0.0001*** **	**0.0001*** **	**<0.0001*** **

P value< 0.05 significant

As well as, the role of curcumin as a protective role against BPA on the sexual hormones, revealed that, could increase the concentration of LH, FSH and testosterone as compared to Bisphenol A treated group, as showed in the table(3)

Table (3): The effect of curcumin vs. BPA on the sexual hormones LH, FSH and testosterone

Parameters	Mean of control	Mean of BPA	Mean of BPA+Curcumin
LH (IU/L)	11.61	2.454	13.92
FSH (ng/ml)	24.99	8.883	31.19
Testosterone (pg/ml)	246.9	40.40	203.4
***P* value**	0.0007**	0.0004**	0.0002***

P value< 0.05 significant

Exposure to BPA affects sexual differentiation, brain development, and social behavior. There is increasing evidence that the ability of BPA to cause reactive oxygen species may have a substantial impact on both its toxicity and its potential to cause cancer [12]. The activity of superoxide dismutase and catalase decreased in groups exposed

to BPA intoxication. Additionally, there was a significant increase in the levels of malondialdehyde . These findings align with the results of Geetha-rathan, who conducted a study on the impact of BPA on the tissues of pregnant rats [13]. The administration of Bisphenol A (BPA) increased the activity of MDA in the treated groups, leading to cognitive dysfunctions and oxidative stress in rats [14]. The rats that were treated to BPA had markedly elevated levels of MDA compared to the rats in the control group ($p < 0.05$) [15].

The presence of bisphenol A, with its estrogenic and anti-androgenic effects, hindered the growth and functioning of Leydig cells. This led to several reproductive diseases such as testicular dysgenesis syndrome, delayed puberty, and subfertility/infertility [16]. The exposure to BPA led to a notable decrease in the levels of FSH compared to the control group[17]. BPA, when it attaches to both estrogen receptors, has the ability to stimulate the ERK1/2 pathway. This pathway hinders the growth of Leydig cells and reduces the production of testosterone [16]. Additionally, Wisniewski et al. discovered that exposure to BPA resulted in significant changes to various hormones. Specifically, the blood concentrations of FSH were reduced by 38%, LH concentrations were decreased by 65%, and testosterone levels were lowered by 98% in the groups treated with Bisphenol A [1].

The decrease in testosterone production by Leydig cells due to Bisphenol A may be directly attributed to a dip in LH serum levels. A mouse that underwent medical intervention[18]. Atabay et al. demonstrated that Curcumin mitigated the impact of BPA and suppressed the antioxidant enzyme system in the host tissues. This resulted in a noteworthy decrease in MDA levels and a significant increase in catalase and SOD levels compared to the rats treated with BPA. Therefore, curcumin partially prevented the adverse effects caused by BPA [19].

The presence of phenolic compounds in curcumin's structures is a crucial element in its ability to scavenge oxygen-derived free radicals that cause cell lipid peroxidation [20]. Curcumin exhibits a protective impact on the enzymes SOD and CAT, which are reduced as a result of BPA induction. Additionally, curcumin decreases lipid peroxidation, specifically MDA. The number 21 is represented by the numeral [21].In the present study, it was found that when curcumin is used together with other drugs, there is a considerable increase in antioxidant enzyme levels and a reduction in oxidative stress.

Bisphenol A is classified as a hazardous chemical and has adverse effects on various organs, including the reproductive system. Using Curcumin as an antioxidant to counteract the effects of BPA has a positive impact by effectively neutralizing the harmful free radicals and maintaining the sexual hormones at their optimal levels.

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