

**SJMLS - 10 (2) - 014****Endocrine Disruptive Effects of Bisphenol 'A' on Estrogen, Insulin, and Thyroxine Levels in Female Wistar Rats**

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**Abstract**

Bisphenol A (BPA), a synthetic compound widely used in the production of plastics and resins, particularly in water bottles, baby bottles, beverage and food containers, has been identified as an endocrine-disrupting chemical. This study investigated the effects of BPA on estrogen, thyroxine (T4), and insulin levels in female Wistar albino rats. The female Wistar rats, weighing 160-200g, were housed under controlled conditions and acclimatized for one week. Twenty rats were divided into four groups: a control group receiving only water, and three experimental groups receiving 20 mg/kg, 50 mg/kg, and 100 mg/kg of BPA daily for three weeks. Blood samples were collected post-administration, and serum levels of insulin, T4, and estrogen were measured using Enzyme-Linked Immunosorbent Assay (ELISA) techniques. The results indicated significant endocrine disruption across all BPA-treated groups. Insulin levels increased significantly with higher BPA doses, while thyroxine and estrogen levels decreased. Specifically, the highest BPA dose (100 mg/kg) led to insulin levels of  $18.91 \pm 2.42$  IU/mL, T4 levels of  $7.06 \pm 2.89$  mg/L, and estrogen levels of  $114.7 \pm 5.69$  IU/mL, compared to the control group values of  $5.61 \pm 1.03$  IU/mL,  $22.46 \pm 5.50$  g/L, and  $300.6 \pm 55.5$  IU/mL, respectively. No significant differences in body weight were observed across the groups. These findings suggest that BPA exposure significantly disrupts endocrine function, particularly concerning insulin, thyroxine, and estrogen regulation causing potential risks for metabolic and reproductive health.

**Keywords:** Bisphenol A, Insulin, Thyroxine

**Introduction**

Bisphenol A (BPA) is a synthetic organic compound which belongs to a class known as diphenylmethane derivatives and bisphenols. It is mainly used as an additive in the production of polycarbonate plastics and epoxy resins. BPA has found widespread application in various industrial products, including plastic containers, linings for canned foods, and thermal papers production (Lukasiewicz *et al.*, 2021).

It has been proved by researchers that human exposure to BPA is prevalent, with individuals being either directly or indirectly exposed to a range of concentrations as the case maybe (Cimmino *et al.*, 2020). The global estimation shows an average intake of approximately 30.76 ng/kg of body weight per day, arising from multiple exposure pathways, which may include dust inhalation, dermal contact, and ingestion directly or indirectly. Although, ingestion is the main or primary route of exposure, which accounts for approximately 90% of most cases, particularly through consumption of canned foods, products packaged in foil, beverages packed plastic containers, and baby food in plastic (Manzoor *et al.*, 2022).

Bisphenol A (BPA) is characterized by its rapid and extensive absorption from the gastrointestinal tract, with dermal absorption also being notably significant, reaching approximately 13% through human skin. A study conducted by Manzoor *et al.* (2022) showed 8.6% penetration rate with maximum concentration of  $0.022 \mu\text{g}/\text{cm}^2$  per hour.

Upon entering the body, BPA is swiftly absorbed in the gastrointestinal tract and subsequently metabolized in both the liver and intestine (Liu *et al.*, 2022). A portion of the ingested BPA is excreted in urine, sweat, or feces in the form of inactive metabolites, specifically bisphenol A sulfate.

BPA is known to accumulate in adipose tissue and is detectable in the biological fluids of the general population. Notably, BPA has been identified in various human tissues, including the placenta, cord blood, amniotic fluid, fetal liver, breast milk, and even in fetal tissues (Dalkan *et al.*, 2020). Its distribution throughout the body is extensive, with the highest concentrations found in the lungs, followed by the kidneys, thyroid, stomach, heart, spleen, testes, liver, and brain (Katiyar *et al.*, 2024). The ratios of organs to serum BPA concentrations for these organs range from 2.0 to 5.8, with an exception for the brain, where the ratio is 0.75 (Oguazu *et al.*, 2020).

The stability of products made with BPA raises alarming environmental concerns, as this compound can easily leach into foods and beverages packed in them, ultimately leading to direct oral ingestion (Nikova *et al.*, 2023).

Biologically, BPA disrupts functions of hormones by altering hormonal balance, which is achieved through its interactions with estrogen-related receptors (ERR). This alteration can result in various health implications, early onset of sexual characteristics (Cimmino *et al.*, 2020). Elevated serum BPA in females, have been associated with significant changes in estradiol (E2) levels, which can cause reproductive complications such as early puberty, menstrual irregularities, a heightened risk of endometriosis, and increase in the rate of infertility.

Investigations have demonstrated that BPA have the ability to interact with multiple nuclear estrogen receptors, including ER $\alpha$  and ER $\beta$ , along with aryl hydrocarbon receptors and peroxisome proliferator-activated receptors, thereby inducing atypical estrogen signaling pathways (Ben *et al.*, 2019). The binding of BPA to ERR $\alpha$  and ERR $\beta$  can elicit various biological responses owing to its capacity to disrupt normal hormonal signaling. Additionally, BPA has been

shown to influence immune system functions through its multi-targeted effects, particularly through alterations in gene expression patterns during neonatal development (Thongkorn *et al.*, 2021). Such alterations have been linked to a decrease in genes that play critical roles in immunomodulation, which may increase the risk of auto-inflammatory responses.

Thyroid hormones are critical for development, growth, and metabolism, particularly concerning neurodevelopment in children (Salazar *et al.*, 2021). Bisphenol A (BPA) possesses estrogen-like properties and is associated with detrimental impacts on reproductive, endocrine, and immune systems. Recent evidence indicates that BPA may disrupt thyroid hormone synthesis, transport, and metabolism through various mechanisms (Sharif *et al.*, 2022).

Thyroid hormones, namely triiodothyronine (T3) and thyroxine (T4), are secreted by the thyroid gland and play a pivotal role in regulating the body's metabolism. BPA has been shown to interfere with normal thyroid function by affecting cellular signaling and gene transcription. In vitro studies suggest that BPA can bind to thyroid hormone receptors TR $\alpha$  and TR $\beta$ , antagonizing the effects of T3 and inhibiting its transcriptional activity (Diri *et al.*, 2024).

BPA exhibits inhibitory activity on thyroid peroxidase (TPO), a critical enzyme involved in T3 and T4 synthesis. Additionally, BPA's in vitro effects on thyroid receptor  $\beta$  (TR $\beta$ ) include repressing TR $\beta$  transcription and displaying antagonistic properties toward this receptor (Toporova & Balaguer, 2020). BPA disrupts the negative feedback mechanism that thyroid hormones exert on TSH release. It is implicated in accelerated embryonic development and influences metamorphosis by affecting T3 signalling pathways. Increasing evidence suggests that exposure to BPA disrupts thyroid function and it alters both circulating and tissue thyroid hormone concentration as substantiated by various epidemiological studies (Yuan *et al.*, 2023).

The pancreas plays a fundamental role in glucose regulation through which insulin and glucagon are produced by the  $\beta$ -cells and  $\alpha$ -cells of the

pancreas respectively. Alteration in the endocrine function of pancreatic would ultimately affect glucose homeostasis and potentially resulting type 2 diabetes and insulin resistance (Campbell & Newgard, 2021).

Estrogen has been known to regulate pancreatic function through its receptor located on pancreatic cells. These interactions have beneficial effects on maintaining insulin sensitivity and  $\beta$ -cell function (Babiloni-Chust *et al.*, 2022). However, reducing level of estrogen will cause glucose intolerance and insulin resistance (De Paoli *et al.*, 2021).

This study stems from growing concerns over the extensive presence of Bisphenol A (BPA) in the environment and its capacity to interfere with various hormonal pathways. Although its estrogen-like activity is well documented, limited research has addressed its simultaneous influence on insulin and thyroid hormones, particularly in females

### Bisphenol A

Bisphenol A used for this study was purchased from Fulcrum Innovation Nigeria Limited Ilorin Kwara State, Nigeria. The chemical identification and authentication (Product NO; B126112, Batch No; OX03704) was done by the staff of industrial chemistry at the Fulcrum Innovation Nigeria Limited. BPA was dissolved in distilled water before administration.

### Ethical Approval

This research was conducted according to the

guide by the National Institute of Health for the care and laboratory use of animals. Ethical approval was obtained from the institutional Review Ethical committee of Kwara State University, Animals were handled in a humane manner, minimizing the risk of suffering (Ref: KWASU/CR&D/REA/2024/0062).

### Experimental Design

A total of 20 rats were randomly divided into four groups of five rats each. Different groups of rats were administered with freshly prepared BPA orally via cannula at specific concentrations between 20 - 100mg/L in water. The animals were treated via oral gavage once daily for three weeks as follows.

Group A was the control taking only water. Group B was administered orally daily 20mg/Kg/day of BPA. Group C was administered daily 50mg/Kg/day of BPA. Group D was administered daily 100mg/Kg/day of BPA. Pre and post treatment body weight was recorded

### Result

#### Comparison of Pre- and Post-Treatment Weight of Rats for the Study

Rats for this study were treated with varied concentration of bisphenol (BPH), and the weights were measured by pre and post administration. As revealed on table 1, there were no significant differences between pre-treatment and post-treatment weight. There was no statistically significant increase in weight in the control groups, 20mg- and 50mg-treated groups. Similarly, there was no statistically significant decrease in the post-treatment weight in the 100mg-treated rats in relation to pre-treatment.

**Table 1: Comparison of Pre- and Post-treatment weight of the rats**

Groups	Pre-weight (Kg)	Post-weight (Kg)	P-value
Negative control	208.25 ± 15.65	228.25 ± 30.09	0.578
20mgBPH	203.09 ± 21.11	235.42 ± 31.66	0.404
50mgBPH	239.12 ± 20.16	242.33 ± 38.64	0.257
100mgBPH	224.34 ± 26.10	211.82 ± 33.04	0.292

The values are mean ± standard deviation, Student t-test was used to compare the means and  $p = 0.005$ .

#### Comparison of Selected Hormonal Parameters Between Negative Control Group and Rats Treated with 20mg BPH/kg BWT

Table 2 shows a comparison of Insulin, T4 and Estradiol between negative control and 20mg/Kg BWT treated BPH. The outcome revealed that there were significant differences in all the parameters.

**Table 2: Comparison of selected Hormonal Parameters between Negative control and rat treated with 20mg/K w BPH**

Parameters	Negative control	20mgBPH	P-value
Insulin (IU/mL)	5.61 ± 1.03	8.08 ± 1.44	0.030*
Estradiol (IU/mL)	300.6 ± 55.5	209.2 ± 58.8	0.001*
T4 (g/L)	22.46 ± 5.50	16.54 ± 3.83	0.000*

The values are mean ± standard deviation, Student t-test was used to compare the means and p = 0.005, NC = negative control, T4 = thyroxine. \* = signify a significant difference.

**Comparison of Selected Hormonal Parameters Between Negative Control Group and Rats Treated with 50mg BPH/kg BWT**

Table 3 shows the comparison of Insulin, T4 and Estradiol between negative control and 50mg/Kg BWT treated BPH. The outcome revealed that there were significant differences in all the parameters.

**Table 3: Comparison of selected Hormonal Parameters between Negative control and rat treated with 50mg/K w BPH**

Parameters	Negative control	50mgBPH	P-value
Insulin (IU/mL)	5.61 ± 1.03	14.50 ± 1.98	0.000*
Estradiol (IU/mL)	300.6 ± 69.5	143.5 ± 34.23	0.000*
T4 (g/L)	22.46 ± 5.50	11.88 ± 3.89	0.000*

The values are mean ± standard deviation, Student t-test was used to compare the means and p = 0.005, NC = negative control, T4 = thyroxine. \* = signify a significant difference.

**Comparison of Selected Hormonal Parameters Between Negative Control Group and Rats Treated With 100mg BPH/kg BWT**

Table 4 shows a comparison of Insulin, T4 and Estradiol between negative control and 1000mg/Kg BWT treated BPH. The outcome revealed that there were significant differences in all the parameters.

**Table 4: Comparison of selected Hormonal Parameters between Negative control and rat treated with 100mg/K w BPH**

Parameters	Negative control	100mgBPH	P-value
Insulin (IU/mL)	5.61 ± 1.03	18.91 ± 2.42	0.000*
Estradiol (IU/mL)	300.6 ± 69.5	114.7 ± 5.69	0.000*
T4 (mg/L)	22.46 ± 5.50	7.06 ± 2.89	0.000*

The values are mean ± standard deviation, Student t-test was used to compare the means and p = 0.005, NC = negative control, T4 = thyroxine. \* = signify a significant difference.

**Correlation Analysis of Parameters of the Rats Treated with Highest (100mg) Dosage Of BPH/kg BWT**

As revealed in table 5, the outcome of correlation analysis of the group of rats treated with 100mg/Kg BWT of BPH. As shown, a strong positive correlation was observed between insulin, T4 and Estradiol whereas a strong negative correlation was observed between other parameters.

**Table 5: Correlation analysis of different parameters in rats treated with highest dosage of BPH**

Correlation		Insulin	Estradiol	T4
<b>Insulin</b>	R			
	P	1		
<b>Estradiol</b>	R	-0.913		
	P	0.000**	1	
<b>T4</b>	R	-0.960	0.916	
	P	0.000**	0.000**	1

Correlation is significant at  $p < 0.05$

### Discussion

The study aimed to explore the effects of BisphenolA (BPA) on the endocrine system by examining changes in insulin, thyroxine (T4), and estrogen levels in female Wistar albino rats. The results provide significant insights into how BPA exposure impacts these hormonal parameters, overall metabolic and reproductive health. The pre- and post-treatment weight analysis revealed no significant differences between the control and BPA-treated groups, suggesting that BPA exposure did not markedly affect the body weight of the rats over the study period. Although there was an observed weight increase in the control, 20mg, and 50mg BPA groups, it was not statistically significant.

The hormonal analysis showed significant disruptions in insulin, T4, and estrogen levels in all BPA-treated groups compared to the control group. In the 20 mg/kg BPA group, insulin level was significantly elevated relative to the control. The 50 mg/kg group exhibited a more pronounced increase, while the 100 mg/kg group showed the highest insulin levels among all groups. These findings suggest a dose-dependent effect of BPA, with increasing exposure leading to hyperinsulinemia. This pattern implies that BPA may interfere with insulin signaling or induce insulin resistance, potentially elevating the risk of metabolic disorders such as diabetes (Yang *et al.*, 2024).

T4 levels were significantly reduced in the 20 mg/kg BPA group and showed a further decline in the 50 mg/kg group. The 100 mg/kg group

exhibited the lowest T4 levels. The progressive reduction in T4 with increasing BPA doses indicates that BPA may impair thyroid function. BPA-induced hypothyroidism could result in a slowed metabolism, developmental challenges, and other physiological dysfunctions (Özel & Rüeegg, 2023).

Estrogen concentrations were significantly diminished in the 20 mg/kg group and declined further in both the 50 mg/kg and 100 mg/kg groups, with the latter showing the lowest levels. This consistent reduction across all treated groups highlights BPA's potential as an endocrine disruptor. Lower estrogen levels can negatively affect reproductive health, potentially leading to infertility, menstrual irregularities, and other estrogen-related disorders.

Correlation analysis revealed strong interrelationships among the hormonal parameters. A notable negative correlation was observed between insulin and both T4 and estrogen levels, suggesting that BPA-induced hyperinsulinemia is associated with concurrent suppression of thyroid and estrogen hormones. These findings underscore the complex and interconnected nature of endocrine disruptions triggered by BPA exposure.

### Conclusion

In conclusion, BPA significantly disrupts insulin, thyroxine, and estrogen levels in female Wistar albino rats, indicating its potential as an endocrine disruptor with substantial health implications. This study adds to the growing

body of evidence advocating for reduced BPA exposure and enhanced regulatory measures.

**Conflict of interest:** The authors declare no conflicts of interest with respect to the research, authorship, and publication of this article.

## Reference

- Akash, M.S.H., Sabir, S., & Rehman, K. (2020). Bisphenol A-induced metabolic disorders: From exposure to the mechanism of action. *Environmental Toxicology and Pharmacology*; **77**: 103373.
- Alonso-Magdalen, P., Roper, A. B., Soriano, S., García-Arévalo, M., Ripoll, C., Fuentes, E. ... & Nadal, Á. (2012). Bisphenol-A acts as a potent estrogen via non-classical estrogen triggered pathways. *Molecular and Cellular Endocrinology*; **355(2)**: 201-207.
- Babiloni-Chust, I., Dos Santos, R. S., Medina-Gali, R. M., Perez-Serna, A. A., Encinar, J. A., Martinez-Pinna, J., ... & Nadal, A. (2022). G protein-coupled estrogen receptor activation by bisphenol-A disrupts the protection from apoptosis conferred by the estrogen receptors ER $\alpha$  and ER $\beta$  in pancreatic beta cells. *Environment International*; **164**: 107250.
- Bala, R., Singh, V., Rajender, S., & Singh, K. (2021). Environment, lifestyle, and female infertility. *Reproductive Sciences*; **28**: 617-638.
- Banerjee, O., Singh, S., Prasad, S. K., Bhattacharjee, A., Seal, T., Mandal, J., ... & Mukherjee, S. (2023). Exploring aryl hydrocarbon receptor (AhR) as a target for Bisphenol-A (BPA)-induced pancreatic islet toxicity and impaired glucose homeostasis: Protective efficacy of ethanol extract of *Centella asiatica*. *Toxicology*; **500**: 153693.
- Ben-Jonathan, N. (2019). Endocrine disrupting chemicals and breast cancer: the saga of bisphenol A. *Estrogen Receptor and Breast Cancer: Celebrating the 60th Anniversary of the Discovery of ER*: 343-377.
- Brown-Grant, K. (2023). The control of TSH secretion. *The pituitary gland* (Butterworth, London 1966).
- Campbell, J. E., & Newgard, C. B. (2021). Mechanisms controlling pancreatic islet cell function in insulin secretion. *Nature Reviews Molecular Cell Biology*; **22(2)**: 142-158.
- Cano, R., Pérez, J. L., Dávila, L. A., Ortega, Á., Gómez, Y., Valero-Cedeño, N. J. & Bermúdez, V. (2021). Role of endocrine-disrupting chemicals in the pathogenesis of non-alcoholic fatty liver disease: a comprehensive review. *International Journal of Molecular Sciences*; **22(9)**: 4807.
- Cano, R., Pérez, J. L., Dávila, L. A., Ortega, Á., Gómez, Y., Valero-Cedeño, N. J., ... & Bermúdez, V. (2021). Role of endocrine-disrupting chemicals in the pathogenesis of non-alcoholic fatty liver disease: a comprehensive review. *International Journal of Molecular Sciences*; **22(9)**: 4807.
- Chaker, L., & Peeters, R. P. (2022). Thyroid-Stimulating Hormone. In *The Pituitary* (pp. 173-207). *Academic Press*.
- Cimmino, I., Fiory, F., Perruolo, G., Miele, C., Beguinot, F., Formisano, P., & Oriente, F. (2020). Potential mechanisms of bisphenol A (BPA) contributing to human disease. *International Journal of Molecular Sciences*; **21(16)**: 5761.
- De Paoli, M., Zakharia, A., & Werstuck, G. H. (2021). The role of estrogen in insulin resistance: a review of clinical and pre-clinical data. *The American Journal of Pathology*; **191(9)**: 1490-1498.
- Diril, H., Karaoglan, M., Çimenci, İ. G., & Ulusal, H. (2024). Effect of Bisphenol-A on Thyroid Hormones and Some Biochemical Parameters in Children with Juvenile Diabetes. *Eastern Journal of Medicine*; **29(1)**: 99-107.
- Farrugia, F., Aquilina, A., Vassallo, J., & Pace, N. P. (2021). Bisphenol A and type 2 diabetes mellitus: a review of epidemiologic, functional, and early life factors. *International Journal of Environmental Research and Public Health*; **18(2)**: 716.
- Kim, H. M., Lee, S. M., Choi, J., Soung, N. K., & Heo, J. D. (2021). Effects of bisphenol A and its alternatives, bisphenol F and tetramethylbisphenol F on osteoclast differentiation. *Molecules*; **26(20)**: 6100.
- Köhrle, J., & Frädlich, C. (2021). Thyroid hormone system disrupting chemicals. *Best Practice & Research Clinical Endocrinology & Metabolism*; **35(5)**: 10156.
- Koutaki, D., Paltoglou, G., Vourdoumpa, A., &

- Charmandari, E. (2021). The impact of bisphenolA on thyroid function in neonates and children: a systematic review of the literature. *Nutrients*; **14(1)**: 168.
- Kowalczyk, M., Piwowarski, J. P., Wardaszka, A., Średnicka, P., Wójcicki, M., &Juszczuk-Kubiak, E. (2023). Application of In Vitro Models for Studying the Mechanisms Underlying the Obesogenic Action of Endocrine-Disrupting Chemicals (EDCs) as Food Contaminants—A Review. *International Journal of Molecular Sciences*; **24(2)**: 1083.
- Kwon, J. A., Shin, B., & Kim, B. (2020). Urinary bisphenol A and thyroid function by BMI in the Korean National Environmental Health Survey (K oNEHS) 2012–2014. *Chemosphere*; **240**: 124918.
- Luo, K., Huang, W., Qiao, L., Zhang, X., Yan, D., Ning, Z., ...& Cheng, J. (2022). Dendrocalamuslatiflorus and its component rutin exhibit glucose-lowering activities by inhibiting hepatic glucose production via AKT activation. *Acta Pharmaceutica Sinica B*; **12(5)**: 2239-2251.
- Maćzka, W., Grabarczyk, M., &Wińska, K. (2022). Can antioxidants reduce the toxicity of bisphenol?. *Antioxidants*; **11(2)**: 413.
- Manzoor, M. F., Tariq, T., Fatima, B., Sahar, A., Tariq, F., Munir, S., ...& Ibrahim, S. A. (2022). An insight into bisphenol A, food exposure and its adverse effects on health: A review. *Frontiers in Nutrition*; **9**:1047827.
- Nesan, D., Sewell, L. C., &Kurrasch, D. M. (2018). Opening the black box of endocrine disruption of brain development: Lessons from the characterization of Bisphenol A. *Hormones and Behavior*; **101**: 50-58.
- Nikova, E. V., Temkov, M., & Rocha, J. M. (2023). Occurrence of meso/micro/nano plastics and plastic additives in food from food packaging. Academic Press. In *Advances in Food and Nutrition Research*; **103**: 41-99.
- Norton, L., Shannon, C., Gastaldelli, A., &DeFronzo, R. A. (2022). Insulin: The master regulator of glucose metabolism. *Metabolism*; **129**: 155142.
- Ohore, O.E., & Zhang, S. (2019). Endocrine disrupting effects of bisphenol A exposure and recent advances on its removal by water treatment systems. A review. *Scientific African*; **5**: e00135.
- Özel, F., & Rüegg, J. (2023). Exposure to endocrine-disrupting chemicals and implications for neurodevelopment. *Developmental Medicine & Child Neurology*; **65(8)**: 1005-1011.
- Salazar, P., Villaseca, P., Cisternas, P., & Inestrosa, N. C. (2021). Neurodevelopmental impact of the offspring by thyroid hormone system-disrupting environmental chemicals during pregnancy. *Environmental Research*; **200**: 111345.
- Sharif, K., Kurnick, A., Coplan, L., Alexander, M., Watad, A., Amital, H., &Shoenfeld, Y. (2022). The putative adverse effects of bisphenol A on autoimmune diseases. *Endocrine, Metabolic & Immune Disorders-Drug Targets*; **22(7)**: 665-676.
- Thongkorn, S., Kanlayaprasit, S., Panjabud, P., Saeliw, T., Jantheang, T., Kasitipradit, K., ...&Sarachana, T. (2021). Sex differences in the effects of prenatal bisphenolA exposure on autism-related genes and their relationships with the hippocampus functions. *Scientific Reports*; **11(1)**: 1241.
- Toporova, L., &Balaguer, P. (2020). Nuclear receptors are the major targets of endocrine disrupting chemicals. *Molecular and Cellular Endocrinology*; **502**: 110665.
- Wang, H., Lei, X., Zhang, Z., Ommati, M. M., Tang, Z., & Yuan, J. (2022). Chronic exposure of bisphenol-A impairs cognitive function and disrupts hippocampal insulin signaling pathway in male mice. *Toxicology*; **472**: 153192.
- Wisniewski, P., Romano, R. M., Kizys, M. M., Oliveira, K. C., Kasamatsu, T., Giannocco, G., ...& Romano, M. A. (2015). Adult exposure to bisphenol A (BPA) in Wistar rats reduces sperm quality with disruption of the hypothalamic–pituitary–testicular axis. *Toxicology*; **329**: 1-9.
- Wu, X., Yang, X., Geng, X., Ji, X., Zhang, X., Yue, H., ...& Sang, N. (2022). Bisphenol A analogs induce cellular dysfunction in human trophoblast cells in a thyroid hormone receptor-dependent manner: in silico and in vitro analyses. *Environmental Science & Technology*; **56(12)**: 8384-8394.
- Yang, Z., Liu, H., Wei, J., Liu, R., Zhang, J., Sun,

- M., ...& Tang, N. J. (2024). Bisphenol mixtures, metal mixtures and type 2 diabetes mellitus: Insights from metabolite pro: 108921. doi: 10.1016/j.envint.2024.108921.
- Yuan, S., Du, X., Liu, H., Guo, X., Zhang, B., Wang, Y., ...&Guo, H. (2023). Association between bisphenolA exposure and thyroid dysfunction in adults: a systematic review and meta-analysis. *Toxicology and Industrial Health*; **39(4)**: 188-203.
- Zhang, X., Guo, N., Jin, H., Liu, R., Zhang, Z., Cheng, C., ...& Lu, X. (2022). Bisphenol A drives di (2-ethylhexyl) phthalate promoting thyroid tumorigenesis via regulating HDAC6/PTEN and c-MYC signaling. *Journal of Hazardous Materials*; **425**: 127911.
- Zou, Z., Harris, L. K., Forbes, K., & Heazell, A. E. (2022). Sex-specific effects of bisphenol A on the signaling pathway of ESRRG in the human placenta. *Biology of Reproduction*; **106(6)**: 1278-1291.

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