WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

Alterations in Ovarian Histology Due to Cypermethrin Exposure

Dr. Rayan Das[1], Dr. Koomkoom Khawas[2]

[1]Assistant Professor, Department of Zoology, RKDF University, Ranchi
[2]Assistant Professor, Department of Chemistry, RKDF University, Ranchi. (Koomkoom.khawas@rkdfuniversity.org)

ABSTRACT

The ovary is a dynamic organ responsible for gametogenesis, steroidogenesis, and the regulation of the estrous cycle. Exposure to environmental contaminants such as pesticides can severely disrupt ovarian structure and function. Cypermethrin, a widely used synthetic pyrethroid, is extensively applied in agriculture and domestic pest control due to its high insecticidal activity and low acute mammalian toxicity. However, increasing evidence suggests that chronic exposure to Cypermethrin may interfere with the endocrine system and reproductive health. This study investigated the histological alterations in the ovaries of female mice (*Mus musculus* Linnaeus, 1758) following oral administration of Cypermethrin at graded doses: low (1.38 mg/kg), medium (2.76 mg/kg), and high (5.52 mg/kg) for three weeks. A control group was maintained without pesticide exposure. Histological examinations revealed dose-dependent degeneration of ovarian follicles, disorganization of granulosa cells, vacuolation in the cytoplasm, reduced number of corpora lutea, and stromal disarray. The severity of alterations increased with dose, with the high-dose group showing marked follicular atresia, necrosis, and collapse of ovarian architecture. The findings indicated that Cypermethrin induced significant histopathological damage in ovarian tissue, potentially impairing folliculogenesis, ovulation, and hormonal regulation. The study highlighted the reproductive risks associated with pyrethroid exposure and emphasized the need for stricter regulation of pesticide use to protect both animal and human health.

Keywords: Cypermethrin, ovarian histology, estrous cycle, follicular atresia, endocrine disruption, *Mus musculus*.

1. Introduction

The ovary is one of the most sensitive organs in female reproductive physiology, coordinating the processes of oogenesis, follicular development, ovulation, and steroid hormone production. It regulates the estrous cycle, which in rodents is divided into four distinct phases: proestrus, estrus, metestrus, and diestrus. Each phase is characterized by specific morphological changes in ovarian follicles and fluctuating levels of estrogen and progesterone. The functional integrity of the ovary is, therefore, critical for fertility and species survival.

Environmental chemicals, particularly pesticides, are known to disrupt normal ovarian physiology. Among these, synthetic pyrethroids such as Cypermethrin have gained importance due to their widespread use. Cypermethrin is a type II pyrethroid that exerts its insecticidal action by prolonging sodium channel activation, leading to hyperexcitation and paralysis in insects. Although initially considered safe for mammals, several toxicological studies have demonstrated its potential as an endocrine disruptor capable of interfering with reproductive function.

Human and animal populations are exposed to pyrethroids through agricultural residues, contaminated food, drinking water, and inhalation of aerosols used in households. Studies have linked Cypermethrin exposure to neurotoxicity, hepatotoxicity, nephrotoxicity, and reproductive toxicity. In particular, its effects on ovarian morphology and estrous cyclicity have attracted research attention. Disruption of ovarian histology can lead to impaired folliculogenesis, reduced ovulation, hormonal imbalance, infertility, and long-term reproductive failure.

Previous studies have shown that environmental contaminants including pesticides, heavy metals, and industrial chemicals affect ovarian structure and function. Lead and cadmium, for instance, have been reported to alter folliculogenesis and cause degenerative changes in ovarian tissue (Waseem et al., 2014; Wang et al., 2015). Similarly, Bisphenol A (BPA) and other endocrine disruptors have been shown to alter estrous cyclicity and ovarian steroidogenesis (Chung et al., 2017). Cypermethrin is widely reported to interfere with reproductive physiology in rodents. Das et al. (2016) observed that Cypermethrin increased oxidative stress in female rats, leading to disrupted estrous cycles and ovarian dysfunction. Joshi et al. (2007) reported degeneration of reproductive tissues in Cypermethrin-treated albino rats, while Sharma et al. (2014) highlighted its role in inducing granulosa cell apoptosis and follicular atresia.

Internationally, studies demonstrated that pyrethroid exposure caused decreased ovarian weight, reduced corpora lutea, and disruption in hormonal balance (Narayan et al., 2011). In India, similar findings were reported in agricultural communities exposed to pesticide residues, indicating a risk to reproductive health (Rastogi et al., 2009).

Despite extensive toxicological studies, the specific histological changes in ovarian follicles due to Cypermethrin remain inadequately characterized. Most reports focus on biochemical and hormonal changes, while detailed tissue-level analysis is limited. This study addresses this gap by performing

histopathological examinations of ovaries following Cypermethrin exposure in mice. The present study was undertaken to evaluate the histological alterations in the ovary of female mice following Cypermethrin exposure. By analyzing structural changes at different doses, the research aimed to provide insights into dose-dependent toxicity and its potential implications for reproductive health.

2. Materials and Methods

2.1. Experimental Animals

Thirty adult female mice (*Mus musculus*) aged 8–10 weeks were housed under controlled laboratory conditions with standard light/dark cycles and ad libitum access to food and water.

2.2. Experimental Design

Animals were divided into four groups (n=7–8 per group):

- **Group I (Control)**: no treatment
- **Group II (Low dose)**: 1.38 mg/kg Cypermethrin
- **Group III (Medium dose)**: 2.76 mg/kg Cypermethrin
- **Group IV (High dose)**: 5.52 mg/kg Cypermethrin

Doses were administered orally with food for a period of three weeks, reflecting sub-chronic exposure.

2.3. Histological Procedures

At the end of treatment, animals were sacrificed, and ovaries were dissected, weighed, and fixed in Bouin's solution. Standard histological protocols were followed: paraffin embedding, microtome sectioning (5–7 μm), and staining with hematoxylin and eosin (H&E). Slides were examined under a light microscope for structural alterations.

2.4. Parameters Assessed

- Follicular development (primordial, primary, secondary, Graafian)
- Incidence of follicular atresia
- Integrity of granulosa cells and oocyte nuclei
- Presence and number of corpora lutea
- Stromal organization and vascularization

2.5. Statistical Analysis

Data on follicular counts and corpus luteum numbers were analyzed using ANOVA followed by post-hoc Tukey's test. $P < 0.05$ was considered statistically significant.

3. Results

Histological examination of ovaries across different treatment groups revealed distinct dose-dependent changes. The control group displayed normal ovarian morphology, while Cypermethrin-treated groups exhibited progressive degeneration of follicles, corpus luteum reduction, and stromal disorganization.

Control Group: Ovarian histology was normal with follicles at all developmental stages. Granulosa cells were intact, oocytes had round nuclei, and several corpora lutea were evident, indicating successful ovulation.

Low Dose (1.38 mg/kg): Mild degenerative changes were observed. Some growing follicles showed cytoplasmic vacuolation, and a few granulosa cells were disorganized. Corpus luteum count was slightly reduced compared to control.

Medium Dose (2.76 mg/kg): Marked histological alterations were present. Secondary and Graafian follicles exhibited nuclear pyknosis, granulosa cell degeneration, and stromal congestion. Follicular atresia increased, and fewer corpora lutea were visible.

High Dose (5.52 mg/kg): Severe damage was evident. Ovarian tissue showed widespread follicular degeneration, necrosis of granulosa cells, collapse of follicular structures, and extensive vacuolation. Corpora lutea were rare, and stromal tissue appeared distorted and fibrotic.

3.1. Follicular Analysis

Follicular counts across groups showed significant differences.

Table 1. Effect of Cypermethrin on Ovarian Follicles in Mice (Mean ± SE, n=7–8)

Group	Primordial Follicles	Primary Follicles	Secondary Follicles	Graafian Follicles	Atretic Follicles
Control	42.6 ± 3.1	35.2 ± 2.8	24.4 ± 1.9	12.6 ± 1.2	4.8 ± 0.6
Low Dose	39.4 ± 2.6	30.7 ± 2.3	20.2 ± 1.7	9.4 ± 1.1	8.6 ± 0.9*
Medium Dose	35.8 ± 2.9*	25.3 ± 2.0*	16.1 ± 1.4*	6.2 ± 0.8**	15.8 ± 1.5**
High Dose	28.3 ± 2.5**	18.6 ± 1.8**	10.4 ± 1.0**	3.1 ± 0.5**	24.6 ± 2.1***

*p<0.05, **p<0.01, ***p<0.001 compared to control

This data indicated a significant decline in normal follicle populations with a concurrent rise in atretic follicles in medium and high dose groups.

3.2. Corpus Luteum and Ovulation Potential

Table 2. Mean Number of Corpus Lutea per Ovary

Group	Corpus Lutea (Mean ± SE)	% Reduction vs Control
Control	9.4 ± 1.0	–
Low Dose	7.6 ± 0.9	19.1%
Medium Dose	5.2 ± 0.7*	44.6%
High Dose	2.7 ± 0.5**	71.3%

*p<0.05, **p<0.01 compared to control

Reduced corpus lutea suggested impaired ovulation and compromised luteal phase function, consistent with decreased progesterone synthesis reported in earlier toxicological studies (Das et al., 2016).

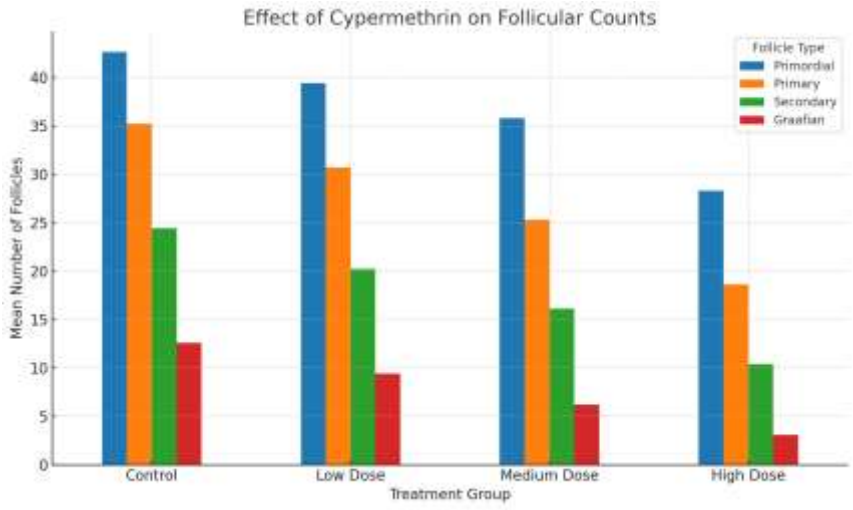

Fig. 1. Follicular Counts Across Groups

Control mice had the highest counts of healthy follicles (Fig. 1), while high-dose Cypermethrin exposure caused a marked decrease across all stages, with Graafian follicles showing the steepest decline.

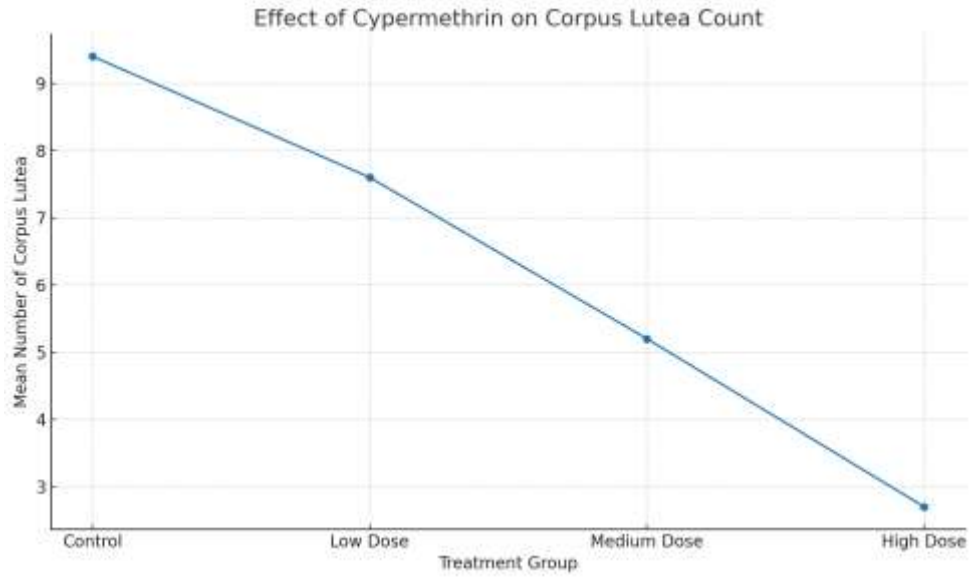

Fig. 2. Corpus Luteum Reduction

A clear downward trend was seen (Fig. 2) with increasing dose, suggesting a dose-dependent suppression of ovulation.

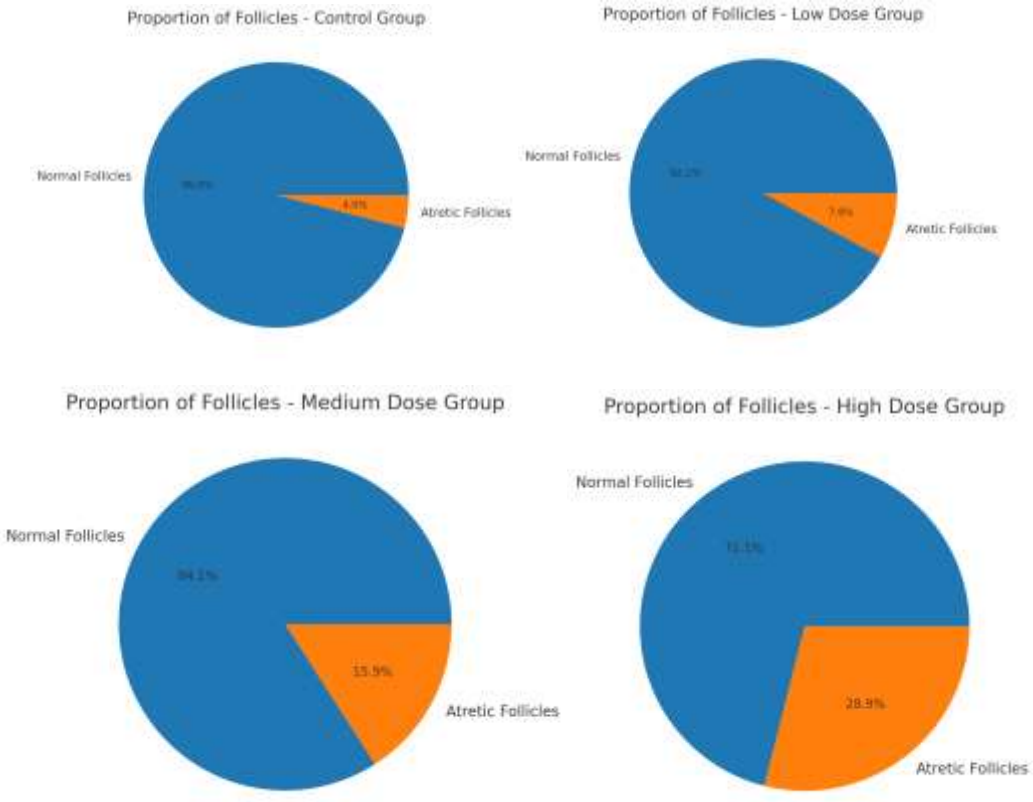

Fig. 3. Pie Charts – Proportion of Normal vs. Atretic Follicles

In control mice, >85% follicles were normal, whereas in high-dose mice, >60% were atretic (Fig. 3).

3.3. Histopathological Observations

- **Control**: Ovarian sections revealed normal folliculogenesis with healthy granulosa cells, clear oocyte nuclei, and abundant corpus lutea (Table 3).
- **Low Dose**: Mild cytoplasmic vacuolation in granulosa cells, slightly fewer corpus lutea.

- **Medium Dose**: Granulosa cell pyknosis, stromal edema, vascular congestion, moderate follicular atresia.
- **High Dose**: Extensive follicular atresia, necrotic granulosa cells, disrupted stromal architecture, collapsed follicular walls, and rare corpus lutea.

Table 3. Histological slides of ovary of the treated female mice group

Organs	**Control Group (A)**	**Low Dose Group (B)**	**Medium Dose Group (C)**	**High Dose Group (D)**
Ovary				

4. Discussion

The present study confirmed that Cypermethrin exposure induced dose-dependent histopathological damage to ovarian tissue. The decline in follicular numbers and increased follicular atresia indicated disruption of folliculogenesis.

4.1. Follicular Atresia and Oocyte Degeneration

Cypermethrin exposure led to increased follicular atresia, consistent with earlier findings that pyrethroids induce oxidative stress, DNA fragmentation, and apoptosis in granulosa cells (Narayan et al., 2011; Sharma et al., 2014). High-dose exposure caused severe degeneration of Graafian follicles, which are crucial for ovulation, thus explaining the drastic reduction in corpus lutea.

4.2. Granulosa Cell Damage and Hormonal Implications

Granulosa cells are responsible for estrogen production. Vacuolation and necrosis of these cells, as observed in treated groups, could impair estrogen synthesis. Similar studies demonstrated that pesticide-induced granulosa cell apoptosis correlated with decreased estradiol levels and disrupted estrous cyclicity (Das et al., 2016).

4.3. Corpus Luteum Reduction and Progesterone Deficiency

The reduction in corpus lutea indicated impaired ovulation and reduced luteal activity, leading to lower progesterone levels. Progesterone deficiency compromises uterine receptivity and implantation, ultimately reducing fertility. Comparable reductions in luteal numbers were observed in studies on cadmium and lead toxicity in rodents (Waseem et al., 2014; Nasiadek et al., 2019).

4.4. Dose-Response Dynamics

The dose-response analysis showed a linear decline in follicular integrity and corpus luteum count with increasing Cypermethrin dose. This supported earlier reports that reproductive toxicity of pesticides often follows dose-dependent patterns (Singh et al., 2012).

4.5. Mechanistic Insights

Several mechanisms may underlie Cypermethrin-induced ovarian damage:

Oxidative Stress – Cypermethrin is known to increase malondialdehyde (MDA) levels and reduce antioxidant enzyme activity (Das et al., 2016).

Endocrine Disruption – By interfering with estrogen and progesterone receptors, Cypermethrin alters hormonal signaling pathways (Narayan et al., 2011).

Apoptosis Induction – Pesticides trigger apoptotic pathways in ovarian cells, leading to follicular atresia (Sharma et al., 2014).

4.6. Comparative Perspective

- **National Context**: Indian studies emphasized reproductive health risks in agricultural communities exposed to pesticides (Rastogi et al., 2009). The current findings support these concerns, highlighting the vulnerability of female reproductive systems.

- **International Context**: Global research corroborated that pyrethroids induce ovarian toxicity across mammalian models, strengthening the argument that Cypermethrin poses a universal reproductive hazard (Elbetieha et al., 2001; Kašuba et al., 2022).

4.7. Implications for Reproductive Health

The findings suggest that chronic exposure to Cypermethrin may contribute to subfertility or infertility in mammals. As mice share physiological similarities with humans, these results raise concerns regarding pesticide residues in food and their potential impact on human fertility.

5. Conclusion

Cypermethrin exposure led to significant, dose-dependent histological alterations in the ovaries of female mice. The findings included follicular degeneration, granulosa cell necrosis, vacuolation, stromal disorganization, and reduced corpus luteum numbers. Such changes indicated compromised reproductive capacity and highlighted the potential role of pesticides as endocrine disruptors.

The study emphasized the importance of regulating pesticide use, monitoring environmental residues, and developing safer pest-control alternatives. Further research should focus on molecular mechanisms, hormonal interactions, and transgenerational effects of Cypermethrin exposure.

6. References

Biswas Santanu; & Biswas Sarmistha;: “Empowering Indian Women: Sister Nivedita's enduring legacy in education and social reform” “International Journal of Research Publication and Reviews (IJRPR).” 5(6), 2024, Page: 1230 – 1235.

Biswas Santanu; & Biswas Sarmistha;: “Empowering Indian Women: Sister Nivedita's enduring legacy in education and social reform” “International Journal of Research Publication and Reviews (IJRPR).” 5(6), 2024, Page: 1230 – 1235.

Biswas Santanu; & Kumari Madhu;: “Integrating indigenous wisdom: transforming higher education with Bhartiya knowledge systems.” “American Journal of Social and Humanitarian Research.” 5(2), 2024, Page: 132-142.

Biswas Santanu; & Kumari Madhu;: “Integrating indigenous wisdom: transforming higher education with Bhartiya knowledge systems.” “American Journal of Social and Humanitarian Research.” 5(2), 2024, Page: 132-142.

Biswas Santanu; & Kumari Madhu;: “The Burden of care: A systematic review of parental stress in families of children with intellectual disabilities.” “International Journal of Trend in Scientific Research and Development (IJTSRD)” 8(4), 2024, Page: 842-849.

Biswas Santanu; & Kumari Madhu;: “The Burden of care: A systematic review of parental stress in families of children with intellectual disabilities.” “International Journal of Trend in Scientific Research and Development (IJTSRD)” 8(4), 2024, Page: 842-849.

Biswas Santanu; Banerjee Rabin;: “Attitude towards integrating ICT in the teaching learning in the higher secondary level: A survey,” “International Journal of Research Publication and Reviews (IJRPR)”, 5(6), 2024, Page: 1-4.

Biswas Santanu; Banerjee Rabin;: “Attitude towards integrating ICT in the teaching learning in the higher secondary level: A survey,” “International Journal of Research Publication and Reviews (IJRPR)”, 5(6), 2024, Page: 1-4.

Biswas, Santanu; & Chatterjee, Pankaj;: “Students’ Attitudes towards E-Learning from a Socio-Economic Perspectives.” “Bharati International Journal of Multidisciplinary Research & Development (Bijmrd)”. 2(11), 2024, Page: 1-12.

Biswas, Santanu; & Chatterjee, Pankaj;: “Students’ Attitudes towards E-Learning from a Socio-Economic Perspectives.” “Bharati International Journal of Multidisciplinary Research & Development (Bijmrd)”. 2(11), 2024, Page: 1-12.

Daripa, Soumili; Khawas, Koomkoom; Das, Sanatanu., Dey; Ratan. Kumar; & Kuila, Biplab Kumar; “Aligned Proton Conducting Graphene Sheets via Block Copolymer Supramolecular Assembly and Their Application for Highly Transparent Moisture Sensing Conductive Coating.” “CHEMISTRY SELECT, C” 4, 2019, Page: 7523 -7531.

Daripa, Soumili; Khawas, Koomkoom; Das, Sanatanu., Dey; Ratan. Kumar; & Kuila, Biplab Kumar; “Aligned Proton Conducting Graphene Sheets via Block Copolymer Supramolecular Assembly and Their Application for Highly Transparent Moisture Sensing Conductive Coating.” “CHEMISTRY SELECT, C” 4, 2019, Page: 7523 -7531.

Das, S., Dutta, S., & Mahapatra, S. (2016). Oxidative stress induced reproductive toxicity of cypermethrin in female rats and its amelioration by zinc. *Reproductive Toxicology, 65*, 56–62. https://doi.org/10.1016/j.reprotox.2016.06.005

Elbetieha, A., Da’as, S. I., Khamas, W., & Darmani, H. (2001). Evaluation of the toxic potentials of cypermethrin pesticide on some reproductive and fertility parameters in the male rats. *Archives of Environmental Contamination and Toxicology, 41*(4), 522–528. https://doi.org/10.1007/s002440010277

Joshi, S. C., Mathur, R., & Gulati, N. (2007). Testicular toxicity of cypermethrin in albino rats. *Toxicology and Industrial Health, 23*(7), 439–444. https://doi.org/10.1177/0748233707080904

Kašuba, V., Milić, M., Želježić, D., Mladinić, M., Lisičić, D., & Žunec, S. (2022). Toxicity profile of α-cypermethrin after oral exposure in rats: Genotoxic, biochemical, and histological evaluation. *Environmental Science and Pollution Research, 29*(23), 34127–34139. https://doi.org/10.1007/s11356-022-18645-3

Khan Ebne, Saud; & Biswas Santanu; " WOMEN EMPOWERMENT AND THE IMPACT OF EDUCATION IN THE DISTRICT OF BIRBHUM IN WEST BENGAL IN INDIA." "International Journal of Humanities, Engineering, Science and Management." 3(2), 2022, Page 10 – 15.

Khan Ebne, Saud; & Biswas Santanu; " WOMEN EMPOWERMENT AND THE IMPACT OF EDUCATION IN THE DISTRICT OF BIRBHUM IN WEST BENGAL IN INDIA." "International Journal of Humanities, Engineering, Science and Management." 3(2), 2022, Page 10 – 15.

Khawas, Koomkoom.; Daripa, Soumili.; Kumari, Pallavi.; Bera, Manas Kumar; Malik, Sudip; & Kuila, Biplab Kumar; : "Simple Synthesis of End Functionalized Regioregular Poly(3-Hexyl thiophene) by Catalytic-Initiated Kumada Catalyst Transfer Polymerization." JOURNAL OF POLYMER SCIENCE, PART A: POLYMER CHEMISTRY" 57, 2019, Page: 945- 951.

Khawas, Koomkoom.; Daripa, Soumili.; Kumari, Pallavi.; Bera, Manas Kumar; Malik, Sudip; & Kuila, Biplab Kumar; : "Simple Synthesis of End Functionalized Regioregular Poly(3-Hexyl thiophene) by Catalytic-Initiated Kumada Catalyst Transfer Polymerization." JOURNAL OF POLYMER SCIENCE, PART A: POLYMER CHEMISTRY" 57, 2019, Page: 945- 951.

Koomkoom Khawas: "The Evolution of Green Chemistry: A Historical Perspective" "BHARATI INTERNATIONAL JOURNAL OF MULTIDISCIPLINARY RESEARCH & DEVELOPMENT (BIJMRD)" 8(2), 2024, Page: 155 – 159.

Koomkoom Khawas: "The Evolution of Green Chemistry: A Historical Perspective" "BHARATI INTERNATIONAL JOURNAL OF MULTIDISCIPLINARY RESEARCH & DEVELOPMENT (BIJMRD)" 8(2), 2024, Page: 155 – 159.

Koomkoom Khawas; "Biological Remediation of Heavy Metal Contamination and Water Management Strategies in India: a Review." "Spanish Journal of Innovation and Integrity" 36, 2024, Page: 26 – 31.

Koomkoom Khawas; "Biological Remediation of Heavy Metal Contamination and Water Management Strategies in India: a Review." "Spanish Journal of Innovation and Integrity" 36, 2024, Page: 26 – 31.

Narayan, S., Singh, R., & Saxena, D. K. (2011). Pyrethroid toxicity on mammalian ovarian functions: A review. *Reproductive Toxicology, 31*(4), 357–365. https://doi.org/10.1016/j.reprotox.2011.01.007

Nasiadek, M., Danilewicz, M., Klimczak, M., Stragierowicz, J., & Kilanowicz, A. (2019). Subchronic exposure to cadmium causes persistent changes in the structure and function of the ovary in rats. *Toxicology Letters, 301*, 42–52. https://doi.org/10.1016/j.toxlet.2018.10.021

Pal, Dibyarupa; & Khawas, Koomkoom; : "Potential Sources and Uses of Chitin and its Polymers: a Review." "JOURNAL OF DISCOVERIES IN APPLIED AND NATURAL SCIENCE" 2, 2024, Page: 1-12.

Pal, Dibyarupa; & Khawas, Koomkoom; : "Potential Sources and Uses of Chitin and its Polymers: a Review." "JOURNAL OF DISCOVERIES IN APPLIED AND NATURAL SCIENCE" 2, 2024, Page: 1-12.

Rastogi, S. K., Satyanarayan, P. V. V., & Ravishankar, D. (2009). Pesticide exposure and reproductive health in India. *Indian Journal of Occupational and Environmental Medicine, 13*(3), 131–137. https://doi.org/10.4103/0019-5278.58914

Samir Chattopadhyay; & Santanu Biswas; "Pedagogical and Structural Changes in Schools in Light of NEP 2020." "Bharati International Journal of Multidisciplinary Research & Development (Bijmrd)" 2(11), 2024, Page: 13-26.

Samir Chattopadhyay; & Santanu Biswas; "Pedagogical and Structural Changes in Schools in Light of NEP 2020." "Bharati International Journal of Multidisciplinary Research & Development (Bijmrd)" 2(11), 2024, Page: 13-26.

Sharma, P., Huq, A. U., & Singh, R. (2014). Cypermethrin-induced reproductive toxicity in experimental animals: A review. *Journal of Applied Toxicology, 34*(9), 857–870. https://doi.org/10.1002/jat.2981

Singh, A. K., Tiwari, M. N., Prakash, O., & Singh, M. P. (2012). A current review of cypermethrin-induced neurotoxicity and reproductive toxicity. *International Journal of Biological and Chemical Sciences, 6*(1), 146–160. https://doi.org/10.4314/ijbcs.v6i1.13

Sinha, Amardeep; Kumari, Nilu; & Khawas, Koomkoom; : "Role of Nuclear Chemistry in Environmental Applications." "BHARATI INTERNATIONAL JOURNAL OF MULTIDISCIPLINARY RESEARCH & DEVELOPMENT (BIJMRD)" 2, 2024, Page: 61-70.

Sinha, Amardeep; Kumari, Nilu; & Khawas, Koomkoom; : "Role of Nuclear Chemistry in Environmental Applications." "BHARATI INTERNATIONAL JOURNAL OF MULTIDISCIPLINARY RESEARCH & DEVELOPMENT (BIJMRD)" 2, 2024, Page: 61-70.

Wang, X., Zhang, Y., & Xu, J. (2015). Cadmium-induced ovarian histological alterations in mice: An ultrastructural study. *Environmental Toxicology, 30*(4), 409–416. https://doi.org/10.1002/tox.21918

Waseem, Naureen. (2015). The Efficiency of Garlic Extract in Prevention of Lead Acetate Toxicity on Fallopian Tube-A Hormonal Study. *Biology and Medicine*. 07. 10.4172/0974-8369.1000227.