
Comparative Toxicity Study of EverX Posterior and SDR Flow+ in Zebrafish Embryo Model

Harish Selvaraj, Ajay Guru Ramesh*

¹Department of Conservative Dentistry and Endodontics, Saveetha University, India

²Department of Conservative Dentistry and Endodontics, Saveetha University, India

Abstract: Objective: This study aimed to assess the potentially toxic effects of EverX Posterior and SDR Flow+ dental materials on zebrafish embryos, using various endpoints such as mortality rate, hatching rate, heart rate, and morphological malformations.

Materials and Methods: Zebrafish embryos were exposed to EverX Posterior and SDR Flow+ dental materials from 4 hours post-fertilization (hpf) to 96 hpf. Parameters including survival, hatching rate, heart rate, and morphological malformations were evaluated. Statistical analysis was performed using one-way ANOVA and Tukey's post hoc test.

Results: EverX Posterior did not cause mortality in zebrafish embryos, while the mortality rate was higher in the SDR Flow+ group. The hatching rate was similar between the EverX Posterior and control groups, but significantly decreased in the SDR Flow+ group. The heart rate of zebrafish embryos exposed to EverX Posterior was not significantly different from the control group, whereas SDR Flow+ resulted in a significant decrease in heart rate. Morphological analysis revealed normal architecture in the EverX Posterior group, while SDR Flow+ treated embryos exhibited malformations and higher mortality.

Conclusion: The study findings suggest that SDR Flow+ had a slightly toxic effect on zebrafish embryos compared to EverX Posterior. Further investigations are warranted to better understand the underlying mechanisms and refine dental materials for enhanced safety and biocompatibility.

Keywords: Zebrafish embryos, composite materials, toxicity testing, EverX Posterior, SDR Flow+, mortality rate, hatching rate, heart rate, morphological malformation

1. Introduction

Zebrafish toxicity testing is a common approach used to assess the potential toxic effects of various substances, including dental materials, on zebrafish embryos and larvae [1–3]. Zebrafish toxicity testing provides valuable insights into the safety and potential risks associated with dental materials before their use in humans [4–6]. In the context of dental materials, zebrafish toxicity testing involves exposing zebrafish embryos or larvae to extracts or direct contact with dental materials or their components [7–9]. The embryos or larvae are typically exposed to different concentrations of the dental material or its leachates, and various endpoints are evaluated to assess toxicity [10–12].

Endpoints commonly evaluated in zebrafish toxicity testing include mortality rate, developmental abnormalities, organ-specific toxicity, and behavioural changes [13–15]. Morphological analysis, histology, gene expression analysis, and behavioural assays are among the methods used to evaluate these endpoints [16–18]. Zebrafish toxicity testing in dental materials allows for the identification of potential adverse effects, such as developmental defects, tissue damage, or neurotoxicity [19–21]. It helps in understanding the underlying mechanisms of toxicity and can guide the refinement of dental materials to enhance their safety and biocompatibility [22–24]. By using zebrafish as a model organism, researchers can efficiently screen multiple dental materials or formulations, assess their toxicity profiles, and prioritize further testing or development [25–27]. Zebrafish toxicity testing provides a valuable tool in early-stage toxicity assessment and contributes to the development of safer dental materials with minimal risks to human health [28–30].

Zebrafish share similarities with humans in terms of tooth development and regeneration. Researchers have used zebrafish to study the genetic and molecular mechanisms involved in tooth development, regeneration, and repair [31–33]. These studies contribute to a better understanding of dental abnormalities and potential strategies

for tooth regeneration in humans. However, zebrafish have been extensively utilized as a model organism in dental research to investigate various aspects of oral health and disease [34–36]. The EverX Posterior is a restorative composite resin that utilizes a resin matrix, silanated e-glass fibers, and inorganic particulate fillers. It is specifically designed as a short fiber-reinforced composite to enhance its mechanical properties. To address the challenges associated with adaptation, flowable restorative composites have been developed as an alternative to high-viscosity resin composites. SDR technology, a patented urethane dimethacrylate structure, has been introduced to reduce polymerization shrinkage and associated stress, claiming minimal overall shrinkage (3.5%) [44-46]. In this study, the EverX Posterior and SDR Flow+ toxic effects were investigated in the zebrafish embryos.

2. Materials and Methods

II a. Origin and Maintenance of Zebrafish

Adult zebrafish (Wild type – AB strain, 4 months old) were purchased from a local aquarist (NSK aquarium, Kolathur, Tamil Nadu, India). The male and female fishes were separated and maintained in our facility under the following condition in a 10 L glass tank: 28.5°C, with a 14/10 h light/dark cycle. The fish were fed three times a day, with live brine shrimp (*Artemia salina*). The fishes were acclimatized for 1 month, later the fishes were utilized for breeding, and embryos were collected and used for the following experiments. The collected embryos are further analyzed under a microscope, unfertilized embryos are discarded, whereas the fertilized embryos are taken in a six-well plate and incubated in an E3 medium [37–39].

Composition of Materials Tested in Study

EverX posterior (everX Posterior GC EUROPE) - Resin matrix, randomly oriented E-glass fibers, and inorganic particulate fillers. The resin matrix contains bisphenol-A-diglycidyl-dimethacrylate (bis-GMA), triethylene glycol dimethacrylate, and polymethylmethacrylate, forming a matrix called semi-interpenetrating polymer network (semi-IPN).

SDR flow+ (SDR; Dentsply-Italy) - The resin matrix contains proprietary modified urethane dimethacrylate resin; TEGDMA; polymerizable dimethacrylate resin; polymerizable trimethacrylate resin; camphorquinone (CQ) photoinitiator; ethyl-4(dimethylamino)benzoate photo accelerator; butylated hydroxytoluene (BHT); fluorescent agent, and UV stabilizer. The filler contains silanated barium-alumino-fluoro-borosilicate glass; silanated strontium alumino-fluoro-silicate glass; surface-treated fumed silicas; ytterbium fluoride; synthetic inorganic iron oxide pigments, titanium dioxide.

A metal mould (2 mm in thickness and 6 mm in diameter) was used to produce ten samples of EverX posterior and SDR Flow+ Composites, for a total of 20 composite disk samples. On the top and bottom of the moulds, a mylar strip was placed, and the cavity was fully filled with composite resin. A thin glass plate was placed over the composite, and using a variable intensity light curing unit (Bluephase NM), the samples were light-cured for 60 seconds. All samples were then finished and polished using Shofu Super Snap Rainbow Technique Kit Ca using a low-speed handpiece (11,000 rpm).

II c Zebrafish embryo toxicity test

For the developmental toxicity assessment studies, 4 hpf embryos were used, and the exposure was carried in a 6-well plate containing untreated larvae as the control, EverX Posterior (EXP) and SDR Flow+ (SDR). Around 15 embryos/well were used with 3 mL of E3 medium. The exposure was non-static and renewed every 24 h with the fresh treatment solution throughout the exposure period (4 hpf to 96 hpf). All the experiments were carried out in triplicates. Parameters such as survival, heart, malformation, and hatching rate were observed during this period, and calculations were presented at the end of 96 hpf [40–43].

II d. Statistical analysis

The data were presented as the mean of triplicates with a standard deviation. GraphPad Prism software (Ver 5.03, CA, USA) was used for statistical analysis. One-way ANOVA was performed and Tukey's post-hoc test was used to find the level of significance between the control and other groups.

3. Result and Discussion

Zebrafish Embryo toxicity test

III a. Mortality and hatching rate

The EverX Posterior did not cause mortality in zebrafish embryos. As shown in Fig. 1, the mortality rate was found to be more than 10% in and SDR Flow+ group. Additionally, the hatching rate was calculated at 48 hpf. It

was observed that 100% of the zebrafish embryo emerged out of their chorions in the control group. However, a similar hatching rate was observed EverX Posterior group and a significant decrease in the hatching rate was observed in the SDR Flow+ group.

III b. Measurement of heart rate

The heart rate of zebrafish embryos was evaluated at 72 hpf, to assess the toxicity of the treatment group. The atrial and ventricular contractions were counted and recorded under a microscope for 1 min and average heart beats per minute were reported. The result shows that the EXP group did not significantly alter the heartbeat rate of the zebrafish embryos when compared to the embryos from the control (untreated) group, while SDR showed a significant decrease in heart rate (Fig. 2).

III c. Morphological malformation

The EXP-treated zebrafish embryos exhibited normal morphological architecture under the microscope (Fig. 3). No malformations such as yolk sac oedema and bent spine were formed in the larvae. Embryos were observed with normal morphology without any deformities when treated with EXP and SDR was observed with dead embryos.

4. Conclusion

The results show that SDR showed a slightly toxic effect on the embryos compared to the EXP when exposed to the zebrafish embryos.

5. Acknowledgement

Nil

References

1. P. Kumar, I. Ajay, G. Sri, S. Chandrakumar, C. Lite, Molecular process of glucose uptake and glycogen storage due to hamamelitannin via insulin signalling cascade in glucose metabolism, *Mol. Biol. Rep.* 47 (2020) 6727–6740. <https://doi.org/10.1007/s11033-020-05728-5>.
2. [2] A. Guru, C. Lite, A.J. Freddy, P. Kumar, M. Pasupuleti, T. Saraswathi, M. Valan, N.A. Al-dhabi, A. Arshad, Intracellular ROS scavenging and antioxidant regulation of WL15 from cysteine and glycine-rich protein 2 demonstrated in zebrafish in vivo model, *Dev. Comp. Immunol.* 114 (2021) 103863. <https://doi.org/10.1016/j.dci.2020.103863>.
3. [3] A. Guru, P.K. Issac, M. Velayutham, N.T. Saraswathi, A. Arshad, J. Arockiaraj, Molecular mechanism of down-regulating adipogenic transcription factors in 3T3-L1 adipocyte cells by bioactive anti-adipogenic compounds, *Mol. Biol. Rep.* 48 (2021) 743–761. <https://doi.org/10.1007/s11033-020-06036-8>.
4. [4] P.K. Issac, C. Lite, A. Guru, M. Velayutham, Tryptophan-tagged peptide from serine threonine-protein kinase of *Channa striatus* improves antioxidant defence in L6 myotubes and attenuates caspase 3 – dependent apoptotic response in zebrafish larvae National Centre for Cell Science, *Fish Physiol. Biochem.* (2021). <https://doi.org/https://doi.org/10.1007/s10695-020-00912-7>.
5. [5] A. Guru, P.K. Issac, N.T. Saraswathi, V.D. Seshadri, G.A. Gabr, J. Arockiaraj, Deteriorating insulin resistance due to WL15 peptide from cysteine and glycine-rich protein 2 in high glucose-induced rat skeletal muscle L6 cells, *Cell Biol. Int.* 45 (2021) 1698–1709. <https://doi.org/10.1002/cbin.11608>.
6. [6] P.K. Issac, R. Karan, A. Guru, R. Pachaiappan, M.V. Arasu, N.A. Al-Dhabi, K.C. Choi, R. Harikrishnan, J.A. Raj, Insulin signaling pathway assessment by enhancing antioxidant activity due to morin using in vitro rat skeletal muscle L6 myotubes cells, *Mol. Biol. Rep.* 48 (2021) 5857–5872. <https://doi.org/10.1007/s11033-021-06580-x>.
7. [7] P.K. Issac, A. Guru, M. Velayutham, R. Pachaiappan, M.V. Arasu, N.A. Al-Dhabi, K.C. Choi, R. Harikrishnan, J. Arockiaraj, Oxidative stress induced antioxidant and neurotoxicity demonstrated in vivo zebrafish embryo or larval model and their normalization due to morin showing therapeutic implications, *Life Sci.* 283 (2021) 119864. <https://doi.org/10.1016/j.lfs.2021.119864>.
8. [8] M. Velayutham, B. Ojha, P.K. Issac, C. Lite, A. Guru, M. Pasupuleti, M.V. Arasu, N.A. Al-Dhabi, J. Arockiaraj, NV14 from serine O-acetyltransferase of cyanobacteria influences the antioxidant enzymes in vitro cells, gene expression against H₂O₂ and other responses in vivo zebrafish larval model, *Cell Biol. Int.* 45 (2021) 2331–2346. <https://doi.org/10.1002/cbin.11680>.
9. [9] P. Sarkar, A. Guru, S. V. Raju, A. Farasani, A.A.A. Oyouni, O.R. Alzahrani, H.A.E. Althagafi, F. Alharthi, K.M. Karupiah, J. Arockiaraj, GP13, an *Arthrospira platensis* cysteine desulfurase-derived

- peptide, suppresses oxidative stress and reduces apoptosis in human leucocytes and zebrafish (*Danio rerio*) embryo via attenuated caspase-3 expression, *J. King Saud Univ. - Sci.* 33 (2021) 101665. <https://doi.org/10.1016/j.jksus.2021.101665>.
10. [10] T. Manjunathan, A. Guru, J. Arockiaraj, P. Gopinath, 6-Gingerol and Semisynthetic 6-Gingerdione Counteract Oxidative Stress Induced by ROS in Zebrafish, *Chem. Biodivers.* 18 (2021) 100374. <https://doi.org/10.1002/cbdv.202100650>.
 11. [11] M. Velayutham, A. Guru, M.V. Arasu, N.A. Al-Dhabi, K.C. Choi, P. Elumalai, R. Harikrishnan, A. Arshad, J. Arockiaraj, GR15 peptide of S-adenosylmethionine synthase (SAME) from *Arthrospira platensis* demonstrated antioxidant mechanism against H₂O₂ induced oxidative stress in in-vitro MDCK cells and in-vivo zebrafish larvae model, *J. Biotechnol.* 342 (2021) 79–91. <https://doi.org/10.1016/j.jbiotec.2021.10.010>.
 12. [12] G. Sudhakaran, A. Guru, B. Hari Deva Muthu, R. Murugan, A. Arshad, J. Arockiaraj, Evidence-based hormonal, mutational, and endocrine-disrupting chemical-induced zebrafish as an alternative model to study PCOS condition similar to mammalian PCOS model, *Life Sci.* 291 (2022) 120276. <https://doi.org/10.1016/j.lfs.2021.120276>.
 13. [13] A. Guru, M. Velayutham, J. Arockiaraj, Lipid-Lowering and Antioxidant Activity of RF13 Peptide From Vacuolar Protein Sorting-Associated Protein 26B (VPS26B) by Modulating Lipid Metabolism and Oxidative Stress in HFD Induced Obesity in Zebrafish Larvae, *Int. J. Pept. Res. Ther.* 28 (2022) 74. <https://doi.org/10.1007/s10989-022-10376-3>.
 14. [14] H.D.M. B, A. Guru, G. Sudhakaran, R. Murugan, A. Arshad, J. Arockiaraj, Double-edged sword role of shrimp miRNA explains an evolutionary language between shrimp-pathogen interactions that unties the knot of shrimp infection, *Rev. Aquac.* 14 (2022) 578–593. <https://doi.org/10.1111/raq.12613>.
 15. [15] N. Prabha, A. Guru, R. Harikrishnan, M.K. Gatasheh, A.A. Hatamleh, A. Juliet, J. Arockiaraj, Neuroprotective and antioxidant capability of RW20 peptide from histone acetyltransferases caused by oxidative stress-induced neurotoxicity in in vivo zebrafish larval model, *J. King Saud Univ. - Sci.* (2022) 101861. <https://doi.org/10.1016/j.jksus.2022.101861>.
 16. [16] M. Velayutham, A. Guru, M.K. Gatasheh, A.A. Hatamleh, A. Juliet, J. Arockiaraj, Molecular Docking of SA11, RF13 and DI14 Peptides from Vacuolar Protein Sorting Associated Protein 26B Against Cancer Proteins and In vitro Investigation of its Anticancer Potency in Hep-2 Cells, *Int. J. Pept. Res. Ther.* 28 (2022). <https://doi.org/10.1007/s10989-022-10395-0>.
 17. [17] G. Sudhakaran, P. Prathap, A. Guru, R. Rajesh, S. Sathish, T. Madhavan, M. V. Arasu, N.A. Al-Dhabi, K.C. Choi, P. Gopinath, J. Arockiaraj, Anti-inflammatory role demonstrated both in vitro and in vivo models using nonsteroidal tetranortriterpenoid, Nimbin (N1) and its analogs (N2 and N3) that alleviate the domestication of alternative medicine, *Cell Biol. Int.* 46 (2022) 771–791. <https://doi.org/10.1002/cbin.11769>.
 18. [18] P.K. Issac, M. Velayutham, A. Guru, G. Sudhakaran, R. Pachaiappan, J. Arockiaraj, Protective effect of morin by targeting mitochondrial reactive oxygen species induced by hydrogen peroxide demonstrated at a molecular level in MDCK epithelial cells, *Mol. Biol. Rep.* (2022) 1–12. <https://doi.org/10.1007/s11033-022-07261-z>.
 19. [19] G. Sudhakaran, A. Guru, B. Haridevamuthu, R. Murugan, A. Arshad, J. Arockiaraj, Molecular properties of postbiotics and their role in controlling aquaculture diseases, *Aquac. Res.* 53 (2022) 3257–3273. <https://doi.org/10.1111/are.15846>.
 20. [20] B. Haridevamuthu, T. Manjunathan, A. Guru, R. Saravana, Hydroxyl containing benzo[b]thiophene analogs mitigates the acrylamide induced oxidative stress in the zebrafish larvae by stabilizing the glutathione redox cycle, *Life Sci.* 298 (2022). <https://doi.org/10.1016/j.lfs.2022.120507>.
 21. [21] A. Guru, G. Sudhakaran, M. Velayutham, R. Murugan, R. Pachaiappan, R.A. Mothana, O.M. Noman, A. Juliet, J. Arockiaraj, Daidzein normalized gentamicin-induced nephrotoxicity and associated pro-inflammatory cytokines in MDCK and zebrafish: Possible mechanism of nephroprotection, *Comp. Biochem. Physiol. Part C Toxicol. Pharmacol.* 258 (2022) 109364. <https://doi.org/10.1016/j.cbpc.2022.109364>.
 22. [22] C. Lite, A. Guru, M.J. Juliet, J. Arockiaraj, Embryonic exposure to butylparaben and propylparaben induced developmental toxicity and triggered anxiety-like neurobehavioral response associated with oxidative stress and apoptosis in the head of zebrafish larvae, *Environ. Toxicol.* (2022). <https://doi.org/10.1002/tox.23545>.
 23. [23] B. Haridevamuthu, T. Manjunathan, A. Guru, Amelioration of acrylamide induced neurotoxicity by benzo [b] thiophene analogs via glutathione redox dynamics in zebrafish larvae Amelioration of acrylamide induced neurotoxicity by benzo [b] thiophene analogs via glutathione

- redox dynamics in zebraf, Brain Res. 1788 (2022) 147941. <https://doi.org/10.1016/j.brainres.2022.147941>.
24. [24] N.S.S. Siddhu, A. Guru, R.C. Satish Kumar, B.O. Almutairi, M.H. Almutairi, A. Juliet, T.M. Vijayakumar, J. Arockiaraj, Pro-inflammatory cytokine molecules from *Boswellia serrate* suppresses lipopolysaccharides induced inflammation demonstrated in an in-vivo zebrafish larval model, Mol. Biol. Rep. (2022) 7425–7435. <https://doi.org/10.1007/s11033-022-07544-5>.
25. [25] R. Murugan, R. Rajesh, A. Guru, B. Haridevamuthu, B.O. Almutairi, M.H. Almutairi, A. Juliet, S. Renganayagi, P. Gopinath, J. Arockiaraj, Deacetyloxyazadiradione Derived from Epoxyazadiradione of Neem (*Azadirachta indica* A. Juss) Fruits Mitigates LPS-Induced Oxidative Stress and Inflammation in Zebrafish Larvae, Chem. Biodivers. 19 (2022). <https://doi.org/10.1002/cbdv.202200041>.
26. [26] G. Sudhakaran, P. Prathap, A. Guru, B. Haridevamuthu, R. Murugan, B.O. Almutairi, M.H. Almutairi, A. Juliet, P. Gopinath, J. Arockiaraj, Reverse pharmacology of Nimbin-N2 attenuates alcoholic liver injury and promotes the hepatoprotective dual role of improving lipid metabolism and downregulating the levels of inflammatory cytokines in zebrafish larval model, Mol. Cell. Biochem. 477 (2022) 2387–2401. <https://doi.org/10.1007/s11010-022-04448-7>.
27. [27] R. Murugan, A. Guru, B. Haridevamuthu, G. Sudhakaran, A. Arshad, J. Arockiaraj, Lantibiotics: an antimicrobial asset in combating aquaculture diseases, Aquac. Int. 30 (2022) 2365–2387. <https://doi.org/10.1007/s10499-022-00908-5>.
28. [28] M. Velayutham, P. Sarkar, G. Sudhakaran, K.A. Al-Ghanim, S. Maboob, A. Juliet, A. Guru, S. Muthupandian, J. Arockiaraj, Anti-Cancer and Anti-Inflammatory Activities of a Short Molecule, PS14 Derived from the Virulent Cellulose Binding Domain of *Aphanomyces invadans*, on Human Laryngeal Epithelial Cells and an In Vivo Zebrafish Embryo Model, Molecules. 27 (2022) 7333. <https://doi.org/10.3390/molecules27217333>.
29. [29] R. Murugan, R. Rajesh, B. Seenivasan, B. Haridevamuthu, G. Sudhakaran, A. Guru, R. Rajagopal, P. Kuppusamy, A. Juliet, P. Gopinath, J. Arockiaraj, Withaferin A targets the membrane of *Pseudomonas aeruginosa* and mitigates the inflammation in zebrafish larvae; an in vitro and in vivo approach, Microb. Pathog. 172 (2022) 105778. <https://doi.org/10.1016/j.micpath.2022.105778>.
30. [30] B. Haridevamuthu, A. Guru, R. Murugan, G. Sudhakaran, R. Pachaiappan, M.H. Almutairi, B.O. Almutairi, A. Juliet, J. Arockiaraj, Neuroprotective effect of Biochanin a against Bisphenol A-induced prenatal neurotoxicity in zebrafish by modulating oxidative stress and locomotory defects, Neurosci. Lett. 790 (2022) 136889. <https://doi.org/10.1016/j.neulet.2022.136889>.
31. [31] G. Sudhakaran, R. Rajesh, A. Guru, B. Haridevamuthu, R. Murugan, Deacetylated nimbin analog N2 fortifies alloxan-induced pancreatic β -cell damage in insulin-resistant zebrafish larvae by upregulating phosphoenolpyruvate carboxykinase (PEPCK) and insulin levels, Toxicol. Appl. Pharmacol. 454 (2022) 116229. <https://doi.org/10.1016/j.taap.2022.116229>.
32. [32] G. Sudhakaran, R. Rajesh, R. Murugan, M. Velayutham, A. Guru, S. Boopathi, S. Muthupandian, P. Gopinath, J. Arockiaraj, Nimbin analog N_2 alleviates high testosterone induced oxidative stress in CHO cells and alters the expression of *Tox3* and *Dennd1a* signal transduction pathway involved in the PCOS zebrafish, Phyther. Res. (2022) 1–13. <https://doi.org/10.1002/ptr.7685>.
33. [33] A. Guru, G. Sudhakaran, M.H. Almutairi, B.O. Almutairi, A. Juliet, J. Arockiaraj, β -cells regeneration by WL15 of cysteine and glycine-rich protein 2 which reduces alloxan induced β -cell dysfunction and oxidative stress through phosphoenolpyruvate carboxykinase and insulin pathway in zebrafish in-vivo larval model, Mol. Biol. Rep. (2022). <https://doi.org/10.1007/s11033-022-07882-4>.
34. [34] M. Singh, A. Guru, G. Sudhakaran, R. Pachaiappan, S. Mahboob, A. Juliet, M. Gobi, J. Arockiaraj, Copper sulfate induced toxicological impact on in-vivo zebrafish larval model protected due to acetin via anti-inflammatory and glutathione redox mechanism Comparative Biochemistry and Physiology, Part C Copper sulfate induced toxicological impact on i, Comp. Biochem. Physiol. Part C. 262 (2022) 109463. <https://doi.org/10.1016/j.cbpc.2022.109463>.
35. [35] A. Guru, J. Arockiaraj, Exposure to environmental pollutant bisphenol A causes oxidative damage and lipid accumulation in Zebrafish larvae: Protective role of WL15 peptide derived from cysteine and glycine-rich protein 2, J. Biochem. Mol. Toxicol. 37 (2023). <https://doi.org/10.1002/jbt.23223>.
36. [36] B. Haridevamuthu, A. Guru, M. Velayutham, P. Snega Priya, A. Arshad, J. Arockiaraj, Long non-coding, a supreme post-transcriptional immune regulator of bacterial or virus-driven immune evolution in teleost, Rev. Aquac. 15 (2023) 163–178. <https://doi.org/10.1111/raq.12709>.
37. [37] A. Guru, T. Manjunathan, G. Sudhakaran, A. Juliet, P. Gopinath, J. Arockiaraj, 6-Gingerdione

- Reduces Apoptotic Conditions in HepG2 Cells and Inhibits Inflammatory Cytokine Gene Expression in Alcoholic Liver Injured Zebrafish Larvae, *Chem. Biodivers.* 20 (2023). <https://doi.org/10.1002/cbdv.202200959>.
38. [38] P. Sarkar, S. V. Raju, M. Velayutham, A. Guru, M. Pasupuleti, E.M. Al Olayan, A.F. Boushra, A. Juliet, J. Arockiaraj, A synthetic antioxidant molecule, GP13 derived from cysteine desulfurase of spirulina, *Arthrospira platensis* exhibited anti-diabetic activity on L6 rat skeletal muscle cells through GLUT-4 pathway, *J. King Saud Univ. - Sci.* 35 (2023) 102450. <https://doi.org/10.1016/j.jksus.2022.102450>.
39. [39] G. Sudhakaran, R. Rajesh, A. Guru, M.V. Arasu, P. Gopinath, J. Arockiaraj, Nimbin analogs N5 and N7 regulate the expression of lipid metabolic genes and inhibit lipid accumulation in high-fat diet-induced zebrafish larvae: An antihyperlipidemic study, *Tissue Cell.* 80 (2023) 102000. <https://doi.org/10.1016/j.tice.2022.102000>.
40. [40] P.S. Priya, A. Guru, R. Meenatchi, B. Haridevamuthu, M. Velayutham, B. Seenivasan, R. Pachaiappan, R. Rajagopal, P. Kuppasamy, A. Juliet, J. Arockiaraj, Syringol, a wildfire residual methoxyphenol causes cytotoxicity and teratogenicity in zebrafish model, *Sci. Total Environ.* 864 (2023) 160968. <https://doi.org/10.1016/j.scitotenv.2022.160968>.
41. [41] Ajay Guru, Gokul Sudhakaran, S. Karthick Raja Namasivayam, Boopathi Seenivasan, Mukesh Pasupuleti, Jesu Arockiaraj, Meivelu Moovendhan, Serine Threonine-Protein Kinase-Derived IW13 Improves Lipid Metabolism via C/EBP- α /SREBP1/FAS Signaling Pathways in HFD-Induced Zebrafish In Vivo Larval Model, *Appl. Biochem. Biotechnol.* (2023). <https://doi.org/10.1007/s12010-023-04480-3>.
42. [42] M. Velayutham, P. Sarkar, K.M. Karuppiyah, P. Arumugam, S. Shajahan, M. Abu Haija, T. Ahamad, M.V. Arasu, N.A. Al-Dhabi, K.-C. Choi, A. Guru, J. Arockiaraj, PS9, Derived from an Aquatic Fungus Virulent Protein, Glycosyl Hydrolase, Arrests MCF-7 Proliferation by Regulating Intracellular Reactive Oxygen Species and Apoptotic Pathways, *ACS Omega.* (2023). <https://doi.org/10.1021/acsomega.3c00336>.
43. [43] J. Narayanan, T. Tamilanban, P.S. Kumar, A. Guru, S. Muthupandian, M.K. Kathiravan, J. Arockiaraj, Role and mechanistic actions of protein kinase inhibitors as an effective drug target for cancer and COVID, *Arch. Microbiol.* 205 (2023) 238. <https://doi.org/10.1007/s00203-023-03559-z>.
44. [44] Sofan E, Sofan A, Palaia G, Tenore G, Romeo U, Migliau G. Classification review of dental adhesive systems: from the IV generation to the universal type. *Ann Stomatol* 2017;8:1–17.
45. [45] Garoushi S, Gargoum A, Vallittu PK, Lassila L. Short fiber-reinforced composite restorations: A review of the current literature. *J Investig Clin Dent* 2018;9:e12330.
46. [46] Lee CI, Yi MD, Gage BM, Yarbrough LN, Kirkwood BJ, Lien W. Post-Cure Polymerization and Depth-of-Cure Behaviors of Dental Bulk-Fill Resin-Based Composites. *Med J (Ft Sam Houst Tex)* 2021:74–82.

Figure 1.

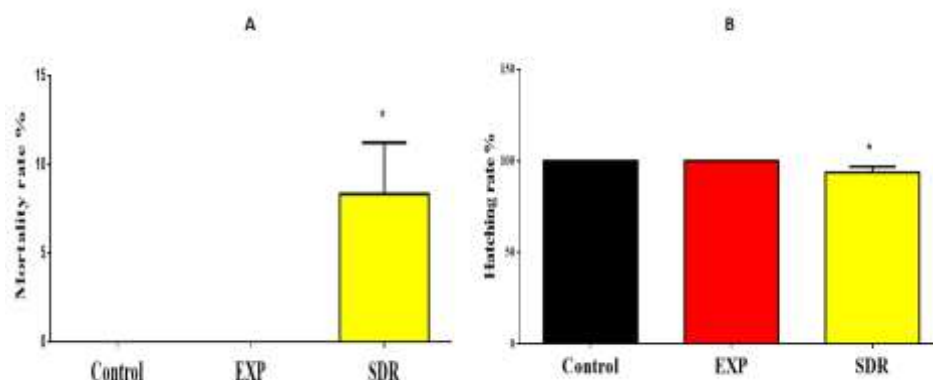


Fig. 1. The Mortality and Hatching rate of zebrafish embryos was investigated after exposure to different groups of EXP and SDR for 24hrs. The * ($p < 0.05$) indicates the significant differences between the control (untreated embryos) and treated group

Figure 2.

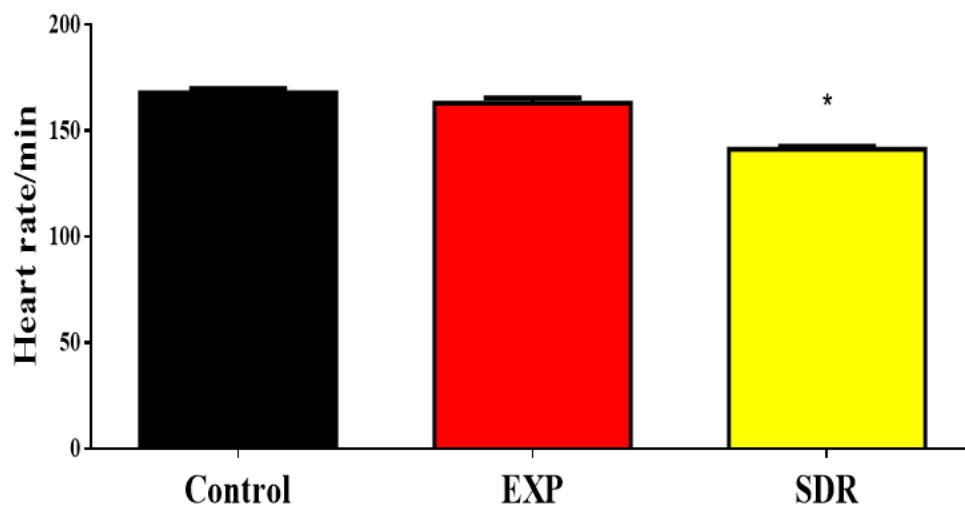


Fig. 2. The Heart rate of zebrafish embryos was investigated after exposure to different groups of EXP and SDR for 24hrs. The * ($p < 0.05$) indicates the significant differences between the control (untreated embryos) and treated group

Figure 3.

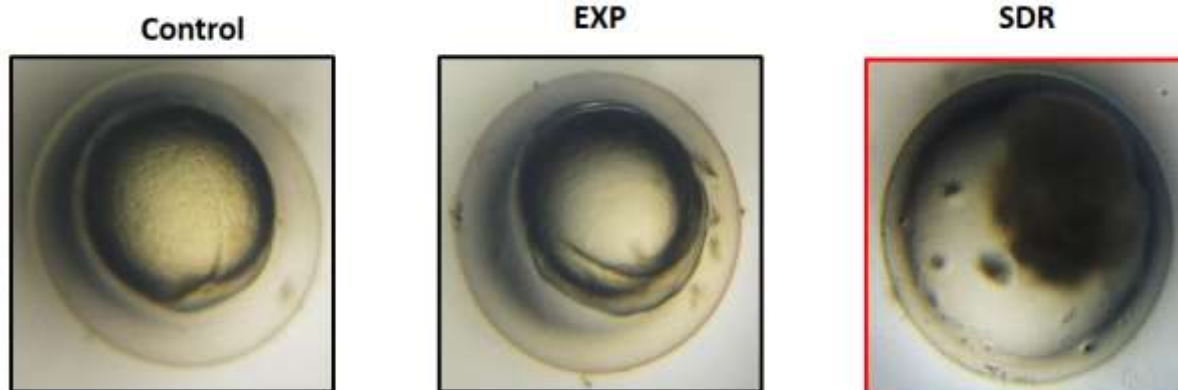


Fig. 3. Microscopic image of embryos after exposure to EXP and SDR. The control was untreated embryos.