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Aspartame Causes Developmental Defects and Teratogenicity in Zebra Fish Embryo: Role of Impaired SIRT1/FOXO3a Axis in Neuron Cells

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Citation: Pandaram, A.; Paul, J.; Wankhar, W.; Thakur, A.; Verma, S.; Vasudevan, K.; Wankhar, D.; Kammala, A.K.; Sharma, P.; Jaganathan, R.; et al. Aspartame Causes Developmental Defects and Teratogenicity in Zebra Fish Embryo: Role of Impaired SIRT1/FOXO3a Axis in Neuron Cells. *Biomedicines* **2024**, *12*, 855. https://doi.org/10.3390/biomedicines12040855

Academic Editor: Marc Ekker

Received: 7 March 2024
Revised: 28 March 2024
Accepted: 28 March 2024
Published: 12 April 2024

Abstract: Aspartame, a widely used artificial sweetener, is present in many food products and beverages worldwide. It has been linked to potential neurotoxicity and developmental defects. However, its teratogenic effect on embryonic development and the underlying potential mechanisms need to be elucidated. We investigated the concentration- and time-dependent effects of aspartame on zebrafish development and teratogenicity. We focused on the role of sirtuin 1 (SIRT1) and Forkhead-box transcription factor (FOXO), two proteins that play key roles in neurodevelopment. It was found that aspartame exposure reduced the formation of larvae and the development of cartilage in zebrafish. It also delayed post-fertilization development by altering the head length and locomotor behavior of zebrafish. RNA-sequencing-based DEG analysis showed that SIRT1 and FOXO3a are involved in neurodevelopment. In silico and in vitro analyses showed that aspartame could target and reduce the expression of SIRT1 and FOXO3a proteins in neuron cells. Additionally, aspartame triggered the reduction of autophagy flux by inhibiting the nuclear translocation of SIRT1 in neuronal cells. The findings suggest that aspartame can cause developmental defects and teratogenicity in zebrafish embryos and reduce autophagy by impairing the SIRT1/FOXO3a axis in neuron cells.

Keywords: aspartame; zebrafish embryos; teratogenicity; neurodevelopment; SIRT1/FOXO3a axis

1. Introduction

Aspartame, an artificial sweetener, has become more popular as an alternative to sugar, particularly among those battling obesity, diabetes, metabolic syndrome, and weight loss management [1,2]. However, there is yet to be definitive proof of its safety to back