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In Vitro and In Vivo Preventive Effects of Thymoquinone against Breast Cancer: Role of DNMT1

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Abstract: Breast cancer (BC) is one of the most common cancers in women and is a major cause of female cancer-related deaths. BC is a multifactorial disease caused by the dysregulation of many genes, raising the need to find novel drugs that function by targeting several signaling pathways. The antitumoral drug thymoquinone (TQ), found in black seed oil, has multitargeting properties against several signaling pathways. This study evaluated the inhibitory effects of TQ on the MCF7 and T47D human breast cancer cell lines and its antitumor activity against BC induced by a single oral dose (65 mg/kg) of 7,12-dimethylbenzanthracene (DMBA) in female rats. The therapeutic activity was evaluated in DMBA-treated rats who received oral TQ (50 mg/kg) three times weekly. TQ-treated MCF7 and T47D cells showed concentration-dependent inhibition of cell proliferation and induction of apoptosis. TQ also decreased the expression of DNA methyltransferase 1 (DNMT1) in both cancer cell types. In DMBA-treated animals, TQ inhibited the number of liver and kidney metastases. These effects were associated with a reduction in DNMT1 mRNA expression. These results indicate that TQ has protective effects against breast carcinogens through epigenetic mechanisms involving DNMT1 inhibition.

Keywords: breast cancer; thymoquinone; metastasis; epigenetics; DNMT1

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1. Introduction

Breast cancer (BC) is a complex disease characterized by distinct biological subtypes and numerous targeted prognostic markers of therapeutic importance [1,2]. In 2012, 1.7 million BC cases and 521,900 deaths were reported [3]. Over 2.3 million (11.7%) new cases and 684,996 (6.9%) mortalities from BC occurred in 2020, and its prevalence is expected to increase to over 3 million new cases and 1 million deaths by 2040, making BC the most common type of malignancy worldwide in women [4]. BC develops through several mechanisms, including epigenetic modifications that mainly involve the