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Master Thesis Defense

Entitled

MOLECULAR MECHANISIMS UNDERLYING THE ANTI-CANCER ACTIVITY OF ARABIC GUM FROM ACACIA SP. IN TRIPLE-NEGATIVE BREAST CANCER CELLS

by

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Date & Venue

2:00 PM

Wednesday, 9th June

Room ..., ... Building

Abstract

Metastatic breast cancer is the leading cause of cancer-related deaths among women worldwide. Triple-negative breast cancer (TNBC) is the most aggressive, accounting for 15-20% of all breast cancer cases. As TNBC cells lack the expression of hormone receptors estrogen receptors (ER) and progesterone receptors (PR) and human epidermal growth factor receptor 2 (HER2), TNBCs are unresponsive to hormonal therapy and often become highly resistant when exposed to standard chemotherapy, which has been identifies as a major obstacle in TNBC treatment. Gum Arabic, a natural

exudate produced from plants, is widely used traditionally for religious, cosmetics as well as medical purposes since ages. Although it is well reported for its biological activities and medical value, no studies have been carried to assess its anticancer potential. In search of new and novel compounds to target TNBCs effectively and less toxicity, this study aims to evaluate the anticancer activity of Gum Arabic extract (GAE) and against breast cancer MDA-MB-231 cell line, a triple-negative human breast cancer cell line, and to elucidate the molecular targets underlying its mechanism of action. The results revealed that GAE inhibits cell proliferation in a concentration- and time-dependent manner. The anti-proliferative effect of GAE was found to be linked to cell cycle arrest at the G1/S phase along with induction of apoptosis confirmed in the cells as suggested by caspase 3/7 activation and cleaved caspase 3 and cleaved PARP detection. Cell cycle inhibitory protein $p21^{WAFA}$ was increased in GAE treated cells compared to untreated cells while cyclin D1 and c-myc were downregulated. Furthermore, we found that Wnt/β-catenin signaling was markedly inhibited and could induce loss of expression of the canonical Wnt-directed targets genes cyclin D1, c-myc, and survivin in MDA-MB-231 cells treated with GAE. In conclusion, GAE inhibits the proliferation of MDA-MD-231 breast cancer cells that is associated with the suppression of Wnt/β-catenin signaling suggesting that Gum Arabic could be a potential new chemotherapeutic agent against highly chemoresistant triple negative breast.

Keywords: *Gum Arabic*, triple-negative breast cancer, apoptosis, cell cycle, cell cycle arrest, anti-breast cancer agent.