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Malami, I.[a j] , Alhassan, A.M.[b] , Ahmed, Q.U.[c] , Shah, S.A.A.[d e] , Umar, M.[f] , Abubakar, M.S.[g] , Imam, M.U.[h j j] , Abubakar, B.[i j j]

5-Methylcoumarin-4β-glucoside mitigated colon tumor progression in mice with AOM/DSS-induced colon carcinogenesis

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[a] Department of Pharmacognosy and Ethnopharmacy, Faculty of Pharmaceutical Sciences, Usmanu Danfodiyo University, Sokoto, PMB, 2346, Nigeria

[b] Department of Pharmaceutical and Medicinal Chemistry, Faculty of Pharmaceutical Sciences, Usmanu Danfodiyo University, Sokoto, PMB, 2346, Nigeria

[c] Department of Pharmaceutical Chemistry, Kulliyyah of Pharmacy, International Islamic University Malaysia, Pahang, Kuantan, 25200, Malaysia

[d] Faculty of Pharmacy, Universiti Teknologi MARA Cagawan Selangor Kampus Puncak Alam, Selangor42300, Malaysia

[e] Att-Ur-Rahman Institute for Natural Product Discovery, Universiti Teknologi MARA Cagawan Selangor Kampus Puncak Alam, Selangor42300, Malaysia

[f] Department of Morbid Anatomy and Forensic Medicine, Faculty of Basic Clinical Sciences, College of Health Sciences, Usmanu Danfodiyo University, Sokoto, PMB, 2346, Nigeria

[g] Department of Veterinary Pathology, Faculty of Veterinary Medicine, Usmanu Danfodiyo University, Sokoto, PMB, 2346, Nigeria

[h] Department of Medical Biochemistry, Faculty of Basic Medical Sciences, College of Health Sciences, Usmanu Danfodiyo University, Sokoto, PMB, 2346, Nigeria

[i] Department of Pharmacology and Toxicology, Faculty of Pharmaceutical Sciences, Usmanu Danfodiyo University, Sokoto, PMB, 2346, Nigeria

[j] Centre for Advanced Medical Research and Training, Usmanu Danfodiyo University, Sokoto, PMB, 2346, Nigeria

Abstract

Context: The in vitro cytotoxicity profile of 5-Methylcoumarin-4β-glucoside (5-MC4βG) has been demonstrated to inhibit the proliferation of HT-29 adenocarcinoma cells. Aim: The need for newer and affordable chemotherapeutic agents is critical. Main methods: We investigated the effect of 5-MC4βG on an azoxymethane /dextran sodium sulfate-induced colon carcinogenesis model in six groups of laboratory BALB/c mice for six weeks. While the first and second groups of mice served as vehicle and disease controls respectively, the third, fourth, and fifth groups were administered oral graded doses (25, 50, and 100 mg/kg) of 5-MC4βG. The sixth group was treated with 5-Flourouracil (15 mg/kg). Key findings: The 100 mg/kg dose of 5-MC4βG upregulated APC mRNA expression by two-fold and downregulated β-catenin mRNA expression by two-fold compared to their respective disease controls. Furthermore, tumorigenic gene transcripts (MDM2, BCL2, CDK1, and cyclin D1) were downregulated by one-fold (except cyclin D1 which was downregulated by two-fold), whereas pro-apoptotic genes (p53, Bax, and Casp3) were upregulated by two-fold following treatment with 100 mg/kg dose of 5-MC4βG. At the metabolic level, the bioactive compound lowered the expression of classical tumor markers; tissue polypeptide antigen, tumor-associated glycoprotein 72, and carcinoembryonic antigen by at least half. Histologically, 5-MC4βG intervention revealed a reduction in neoplastic cells associated with cellular necrosis. Significance: 5-MC4βG reduced colon carcinogenesis in mice. Thus, this compound may be a promising candidate for colorectal cancer chemotherapy. Further development of 5-MC4βG will hopefully lead to the development of a potential anti-colon cancer drug candidate. © 2024 The Author(s)

Author Keywords

Azoxymethane; Carcinogenesis; Chemotherapy; Colorectal cancer; Dextran sodium sulfate

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Correspondence Address
Abubakar B.; Centre for Advanced Medical Research and Training, Sokoto, Nigeria; email: abubakar.bilyaminu@udusok.edu.ng

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