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Investigation of potassium channel modulation by flavonoids in a prostate cancer cell line: functional role of BKCa channels

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Prostate cancer is one of the most common malignancies in men, and its incidence increases with age. Ongoing research aims to elucidate the mechanisms of prostate cancer progression and develop more effective therapeutic strategies. Baicalein and quercetin are flavonoids known to have anticancer effects. In this study, we investigated the effects of these flavonoids on potassium ion currents in the prostate cancer cell line Du145 using whole-cell patch clamp electrophysiology and examined the effects of specific ion channel inhibitors. The expression of calcium-activated (KCa) and voltage-dependent (Kv) potassium channels was confirmed by RT-PCR. Electrophysiological recordings showed that baicalein and quercetin activated outward potassium currents with a flashing pattern. These currents were significantly inhibited by iberiotoxin (IBX), a selective blocker of large-conductance calcium-activated potassium (BKCa) channels, and tetraethylammonium (TEA), a broad-spectrum potassium channel inhibitor. Interestingly, combined treatment with flavonoids and ion channel inhibitors had minimal effects on flavonoid-induced apoptosis, mitochondrial depolarization, or inhibition of cell migration. Moreover, flavonoid treatment alone had limited effects on cell proliferation. These results suggest that BKCa channels are functionally expressed in Du145 prostate cancer cells and respond to flavonoid modulation, but may play only a minor role in regulating key cancer-related cellular processes under the conditions tested. Further studies are needed to clarify the therapeutic potential of targeting BKCa channels in prostate cancer.

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A natural therapeutic approach to fibrocystic breast disease: antiproliferative effects of phenolic cocktail and metformin on a fibrocystic breast cell line model

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Fibrocystic breast disease is the most prevalent benign breast condition in women of reproductive age, triggered by hormonal fluctuations and characterised by increased breast density, lumps, dimpled skin, or nipple discharge. Severe cases may require hormone therapy or surgery. Without appropriate preventive measures, affected women are at risk of developing malignant tumours. As a natural approach, polyphenols are recognised as non-toxic to healthy cells, exhibiting minimal or no side effects, antioxidant and antiproliferative properties. Antidiabetics are of interest due to their potential to affect cellular energy homeostasis in hormone-sensitive tissues, such as breast tissue, by maintaining glycemic control. Metformin, the most common antidiabetic drug, has been observed to indirectly activate the PPARγ pathway and has been hypothesised to be able to affect malignancies by inducing apoptotic or antiproliferative signals. In this study, the cytotoxic effects of metformin hydrochloride (MetHCl), a patented polyphenolic cocktail (PFK^{5120}), and their combination (MIX) on a human fibrocystic breast epithelial cell line (MCF10A) were investigated. The potential of these substances to induce cell death in fibrocystic breast model was evaluated using the WST8 assay. Statistical analysis was performed using a two-way ANOVA test. MCF10A cells demonstrated a time-dependent cytotoxic response to MetHCl, with the highest toxicity observed at 96 h. The cytotoxic effect of PFK^{5120} was significant at all time points, even at low doses. Furthermore, the combination of both compounds significantly increased toxicity to MCF10A cells in a dose-dependent manner, similar to the effects of MetHCl alone ($p < 0.0001$). The findings of this study underscore the synergistic impacts of the combined utilization of polyphenols and Metformin in impeding cellular proliferation within fibrocystic breast models. Further exploration into the therapeutic potential of these compounds is warranted.

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Role of circadian rhythm disruption by clock gene mutations in lynch syndrome-associated colorectal cancer

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Circadian rhythm, the internal clock of living beings, regulates 24-hour biological cycles, and physiological activities like DNA repair. Little is known about the role of circadian rhythm disruptions in Lynch syndrome-related cancers. This study evaluates how CLOCK and MMR mutations interact to affect Lynch syndrome-related cancers. It discusses how chronotherapy, which times treatments according to circadian rhythm, can improve outcomes. The sample consists of 24 Lynch syndrome patients diagnosed with cancer at Marmara University Prof. Dr. Asaf Ataseven Hospital. After Ethics Committee Approval, a retrospective, anonymous study was conducted using medical records and Clinical Exome Sequencing (CES) panel. CLOCK, PER1, PER2, MLH1, PMS2, MSH2, and MSH6 genes were screened in CES. SOPHIA DDM was used for genomic analysis, and IBM SPSS for statistics. Chi-square test, independent t-test, and Pearson correlation were utilized ($p < 0.05$) 19 CLOCK gene variants were detected (8 PER1, 8 PER2, 3 CLOCK). PER2 c.1995G>A synonymous variant significantly increased in younger patients (mean = 50) compared to noncarriers (mean = 60; $p = 0.003$). No significant gender differences were observed among variants ($p > 0.05$). Among variant trends, PER2 c.1992G>A and CLOCK c.623C>G were the most commonly detected; each was present in colorectal, gastric, and endometrial cancers. PER2 c.3600C>T variant was only seen in colorectal cancers. Colorectal cancers were evaluated as the highest variant

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