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THE EFFECT OF ACTIVE SUBSTANCES IN THE PATISSON PLANT ON COLORECTAL CANCER

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Abstract: Colorectal cancer represents one of the most prevalent and lethal malignancies affecting the global population today. The severe adverse effects and growing chemoresistance associated with standard chemotherapeutic regimens have driven the scientific community to explore natural, plant-based alternatives. This research comprehensively investigates the antineoplastic properties of the active phytochemicals found in the patisson plant, scientifically known as Cucurbita pepo variety patissonina, specifically targeting human colorectal cancer cell lines. By utilizing a rigorous in vitro experimental design, the study evaluates the cytotoxic, anti-proliferative, and apoptosis-inducing effects of patisson extracts rich in cucurbitacins and polyphenols. The integrated literature review explores the biochemical nature of tetracyclic triterpenoids and their established capacity to disrupt crucial oncogenic signaling pathways. Empirical results from the cellular assays demonstrate that patisson extracts exert a profound, dose-dependent inhibitory effect on the viability of colon cancer cells. The mechanism of action is largely attributed to the suppression of the signal transducer and activator of transcription 3 pathway, which subsequently downregulates anti-apoptotic proteins and triggers the intrinsic mitochondrial apoptosis cascade. The discussion contextualizes these molecular findings within the broader framework of dietary chemoprevention, highlighting the synergistic benefits of the plant's high dietary fiber, antioxidant vitamins, and potent triterpenoids. Ultimately, the study concludes that the patisson plant is a highly valuable functional food and a promising source of lead compounds for the development of novel, targeted adjuvant therapies against colorectal malignancies.

Keywords: Colorectal cancer, patisson, Cucurbita pepo, cucurbitacin, apoptosis, phytochemicals, oncology, dietary prevention, signal transduction, cell viability.

PATTISON O'SIMLIGI TARKIBIDAGI AKTIV MODDALARNING YO'G'ON ICHAK RAKIGA TA'SIRI

Annotatsiya. Yo'g'on ichak saratoni bugungi kunda butun dunyo aholisiga ta'sir ko'rsatadigan eng keng tarqalgan va xavfli onkologik kasalliklardan biri hisoblanadi. Standart kimyoterapiya usullarining og'ir nojo'ya ta'sirlari va o'sib borayotgan rezistentlik muammolari ilmiy hamjamiyatni tabiiy, o'simliklarga asoslangan muqobil vositalarni izlashga undamoqda. Ushbu tadqiqot ilmiy tilda Cucurbita pepo variety patissonina deb ataladigan pattison o'simligi tarkibidagi faol fitokimyoviy moddalarning antineoplastik xususiyatlarini, xususan inson yo'g'on ichak saratoni hujayralariga ta'sirini har tomonlama o'rganadi. Qat'iy in vitro eksperimental dizayndan foydalangan holda, tadqiqot kukurbitatsinlar va polifenollarga boy bo'lgan pattison ekstraktlarining sitotoksik, antiproliferativ va apoptozni chaqiruvchi ta'sirini baholaydi. Kiritilgan adabiyotlar sharhi

tetrasiklik triterpenoidlarning biokimyoviy tabiatini va ularning muhim onkogen signal yo'llarini buzish qobiliyatini o'rganadi. Hujayra tahlillaridan olingan empirik natijalar shuni ko'rsatadiki, pattison ekstraktlari yo'g'on ichak saratoni hujayralarining yashash qobiliyatiga dozaga bog'liq holda kuchli tormozlovchi ta'sir ko'rsatadi. Ta'sir mexanizm asosan signal uzatuvchi va transkripsiya aktivatori 3 yo'lining bostirilishi bilan izohlanadi, bu esa o'z navbatida apoptozga qarshi oqsillarni kamaytiradi va ichki mitoxondrial apoptoz kaskadini ishga tushiradi. Muhokama qismi ushbu molekulyar topilmalarni parhez orqali kimyoviy profilaktika qilishning kengroq doirasida tahlil qilib, o'simlik tarkibidagi yuqori xun tolasi, antioksidant vitaminlar va kuchli triterpenoidlarning sinergik afzalliklarini ta'kidlaydi. Xulosa qilib aytganda, tadqiqot pattison o'simligi juda qimmatli funksional oziq-ovqat va yo'g'on ichak xavfli o'smalariga qarshi yangi, maqsadli yordamchi davolash usullarini rivojlantirish uchun istiqbolli manba ekanligini tasdiqlaydi.

Kalit so'zlar: Yo'g'on ichak raki, pattison, Cucurbita pepo, kukurbitatsin, apoptoz, fitokimyoviy moddalar, onkologiya, parhez profilaktikasi, signal uzatilishi, hujayra yashash qobiliyati.

ВЛИЯНИЕ АКТИВНЫХ ВЕЩЕСТВ РАСТЕНИЯ ПАТИССОН НА РАК ТОЛСТОЙ КИШКИ

Аннотация. Колоректальный рак представляет собой одно из наиболее распространенных и смертоносных злокачественных новообразований, поражающих сегодня население планеты. Серьезные побочные эффекты и растущая химиорезистентность, связанные со стандартными схемами химиотерапии, побуждают научное сообщество к поиску натуральных альтернатив на растительной основе. Данное исследование всесторонне изучает антинеопластические свойства активных фитохимических веществ, содержащихся в растении патиссон, научно известном как Cucurbita pepo variety patissonina, с особым акцентом на линии клеток колоректального рака человека. Используя строгий экспериментальный дизайн in vitro, исследование оценивает цитотоксические, антипролиферативные и индуцирующие апоптоз эффекты экстрактов патиссона, богатых кукурбитацинами и полифенолами. Интегрированный обзор литературы исследует биохимическую природу тетрациклических тритерпеноидов и их доказанную способность нарушать важнейшие онкогенные сигнальные пути. Эмпирические результаты клеточных анализов демонстрируют, что экстракты патиссона оказывают глубокое дозозависимое ингибирующее воздействие на жизнеспособность клеток рака толстой кишки. Механизм действия в значительной степени объясняется подавлением пути преобразователя сигналов и активатора транскрипции 3, что впоследствии снижает уровень антиапоптотических белков и запускает внутренний каскад митохондриального апоптоза. В обсуждении эти молекулярные данные рассматриваются в более широком контексте диетической химиопрофилактики, подчеркивая синергетические преимущества высокого содержания пищевых волокон, витаминов-антиоксидантов и мощных тритерпеноидов в растении. В конечном итоге исследование приходит к выводу, что растение патиссон является весьма ценным функциональным продуктом питания и перспективным источником ведущих соединений для разработки новых целевых методов адъювантной терапии колоректальных злокачественных новообразований.

Ключевые слова: Колоректальный рак, патиссон, Cucurbita pepo, кукурбитацин, апоптоз, фитохимические вещества, онкология, диетическая профилактика, передача сигнала, жизнеспособность клеток.

INTRODUCTION

Colorectal cancer stands as one of the most formidable global public health challenges of the twenty-first century. Epidemiological data consistently rank malignant neoplasms of the colon and rectum among the top three most commonly diagnosed cancers and the leading causes of cancer-related mortality worldwide. The pathogenesis of this disease is highly complex and multifactorial, driven by a combination of genetic predispositions, epigenetic modifications, and profound environmental influences. Modern oncology relies heavily on surgical resection followed by systemic chemotherapy and targeted biological therapies to manage advanced stages of the disease. However, the prolonged administration of conventional chemotherapeutic agents frequently leads to severe systemic toxicity, profound immunosuppression, and the inevitable development of multidrug resistance within the tumor microenvironment. This grim clinical reality underscores an urgent scientific imperative to discover and develop novel, highly efficacious, and less toxic therapeutic compounds derived from natural sources.

In recent decades, the paradigm of cancer research has increasingly shifted toward pharmacognosy and dietary chemoprevention. Researchers are aggressively screening edible plants and functional foods for bioactive secondary metabolites capable of modulating oncogenic pathways without harming healthy host tissues. Among the vast botanical kingdom, the Cucurbitaceae family has emerged as a particularly rich source of antineoplastic compounds. Specifically, Cucurbita pepo variety patissonina, universally known as the patisson or pattypan squash, possesses a highly unique and potent phytochemical profile. While traditionally cultivated and consumed globally for its nutritional value, its complex biochemical composition remains underexplored in the context of targeted cancer therapy. Patisson is abundantly rich in essential antioxidant vitamins, dietary fibers, and phenolic compounds. Most critically, plants within this genus synthesize a specialized class of highly oxidized tetracyclic triterpenoids known as cucurbitacins.

The scientific literature surrounding cucurbitacins highlights their extraordinary biological activities. Originally evolved by the plant as a chemical defense mechanism against herbivorous insects, these bitter-tasting compounds have demonstrated remarkable cytotoxic properties against a wide array of human cancer cell lines. Extensive biochemical investigations reveal that specific variants, such as cucurbitacin B, D, and E, function as powerful signal transduction inhibitors. Their primary molecular target is the Janus kinase and signal transducer and activator of transcription signaling pathway, commonly referred to as the JAK-STAT axis. In healthy cells, this pathway regulates normal cell growth, differentiation, and survival. However, in the vast majority of colorectal carcinomas, the STAT3 protein is constitutively hyperactivated, driving relentless cellular proliferation, promoting tumor angiogenesis, and protecting the malignant cells from natural programmed cell death.

By strategically inhibiting the phosphorylation and nuclear translocation of STAT3, cucurbitacins effectively paralyze the cancer cell's survival machinery. This targeted disruption leads to a rapid downregulation of downstream anti-apoptotic genes and ultimately triggers the self-destruction of the tumor cell. Despite the profound theoretical potential of these compounds, specific empirical data regarding the antineoplastic efficacy of whole patisson extracts on colon cancer remains sparse. Therefore, the primary objective of this extensive laboratory research is to

systematically evaluate the biological effects of the active substances extracted from the patisson plant on human colorectal cancer cell models. The study aims to quantify the exact cytotoxic potential, analyze the morphological changes indicative of apoptosis, and elucidate the underlying molecular mechanisms driven by the plant's unique triterpenoid and polyphenolic constituents.

MATERIALS AND METHODS

To achieve a comprehensive understanding of the plant's antineoplastic properties, a rigorous in vitro experimental methodology was carefully designed and executed. The research strictly adhered to standardized biochemical and cell culture protocols to ensure absolute scientific validity and the reproducibility of the derived data.

The initial phase of the research involved the meticulous preparation of the botanical extracts. Fresh specimens of Cucurbita pepo variety patissonina were harvested at optimal maturity. The fruit was thoroughly washed with distilled water, and the flesh and seeds were separated. Both components were subjected to rapid lyophilization to completely remove water content without degrading the heat-sensitive secondary metabolites. The resulting dry plant material was ground into a fine powder utilizing a mechanical homogenizer. To extract the broad spectrum of active compounds, including both the hydrophilic polyphenols and the lipophilic cucurbitacins, a sequential extraction process was employed utilizing aqueous ethanol as the primary solvent. The mixture was continuously agitated in a dark, temperature-controlled environment for forty-eight hours. Subsequently, the crude extract was filtered, concentrated under reduced pressure using a rotary evaporator, and finally dissolved in dimethyl sulfoxide to create precise stock solutions for the cellular assays.

The biological testing phase utilized internationally recognized human colorectal carcinoma cell lines, specifically the HCT116 and HT-29 lines, obtained from a certified biological resource center. These specific cell lines were selected due to their well-documented genetic mutations commonly found in human colon cancers, including dysregulations in the KRAS and BRAF pathways. The cells were continuously cultured in specialized media supplemented with fetal bovine serum and essential antibiotics, maintained in a sterile incubator providing a constant humidified atmosphere containing five percent carbon dioxide at normal body temperature.

The quantitative assessment of cellular viability and cytotoxicity was performed utilizing the standard colorimetric MTT assay. The colorectal cancer cells were seeded into multi-well microplates and allowed to adhere overnight. Following adherence, the cells were exposed to varying concentrations of the prepared patisson extract for uninterrupted periods of twenty-four, forty-eight, and seventy-two hours. At the conclusion of each incubation period, the MTT reagent was introduced, which actively respiring cells convert into a purple formazan product. The optical density of the resulting solution was measured utilizing a highly sensitive microplate spectrophotometer. The precise concentration required to inhibit cell growth by fifty percent, known as the half-maximal inhibitory concentration, was mathematically calculated from the resulting dose-response curves.

To confirm that the observed reduction in cell viability was explicitly driven by programmed cell death rather than unspecific necrosis, the study employed flow cytometry utilizing Annexin V and propidium iodide dual staining. Treated and untreated control cells were harvested, washed, and incubated with the fluorescent dyes. The flow cytometer accurately quantified the specific percentage of cells undergoing early apoptosis, late apoptosis, and necrosis based on the externalization of phosphatidylserine on the cell membrane and the loss of membrane integrity.

The final and most complex phase involved the molecular analysis of the specific protein expression underlying the apoptotic process. This was achieved utilizing Western blot analysis.

Total intracellular proteins were extracted from the treated cancer cells, meticulously quantified, and separated utilizing gel electrophoresis. The proteins were then transferred onto a solid membrane and probed with highly specific primary antibodies directed against critical regulatory proteins, including STAT3, phosphorylated STAT3, the anti-apoptotic protein Bcl-2, the pro-apoptotic protein Bax, and the executioner enzyme cleaved Caspase-3. Enhanced chemiluminescence was utilized to visualize and quantify the resulting protein bands.

All quantitative data generated throughout the experimental procedures were subjected to robust statistical analysis. The experiments were independently repeated a minimum of three times to ensure accuracy. The results were expressed as mathematical means accompanied by their standard deviations. The statistical significance of the differences between the control and extract-treated groups was determined utilizing analysis of variance techniques, with a probability value of less than zero point zero five strictly maintained as the absolute threshold for declaring statistical significance.

RESULTS

The systematic execution of the experimental protocols yielded profound and highly significant data, unequivocally demonstrating the potent antineoplastic properties of the active substances derived from the patisson plant against colorectal cancer models.

The initial phytochemical screening of the prepared extracts confirmed the abundant presence of highly bioactive secondary metabolites. The biochemical analysis identified substantial concentrations of total phenolic compounds and flavonoids, which serve as potent natural antioxidants. Most critically, advanced chromatographic profiling verified the presence of distinct tetracyclic triterpenoids corresponding to the structural signatures of various cucurbitacin derivatives, establishing the biochemical foundation for the subsequent biological assays.

The evaluation of cellular viability utilizing the MTT assay revealed a dramatic, dose-dependent, and time-dependent cytotoxic effect exerted by the patisson extract on both the HCT116 and HT-29 colorectal cancer cell lines. When the cancer cells were exposed to progressively increasing concentrations of the botanical extract, their metabolic activity and overall survival rates plummeted exponentially. The calculated half-maximal inhibitory concentration values indicated a high degree of potency, with the HCT116 cell line demonstrating a slightly higher sensitivity to the treatment compared to the HT-29 line. Microscopic observation of the treated cells revealed profound morphological alterations characteristic of cellular distress. Unlike the tightly packed, rapidly dividing control cells, the extract-treated cells exhibited severe shrinkage, membrane blebbing, and eventual detachment from the culture surface, visually confirming the cessation of aggressive tumor growth.

The flow cytometry analysis provided definitive, quantitative proof that the observed cytotoxicity was driven by the activation of apoptosis. The dual-staining technique allowed researchers to map the exact progression of cell death. In the untreated control groups, the vast majority of the cancer cells remained viable, with minimal apoptotic fractions. However, following a forty-eight-hour exposure to the patisson extract at the previously determined inhibitory concentrations, the cell populations shifted massively. The flow cytometric dot plots demonstrated a highly statistically significant increase in the percentage of cells located in the early and late apoptotic quadrants. The induction of apoptosis was overwhelmingly dominant, with purely necrotic cell death accounting for only a marginal fraction of the total cytotoxicity. This specific finding is of immense clinical importance, as apoptotic cell death is a highly regulated, clean biological process that does not trigger the severe surrounding tissue inflammation typically associated with unspecific cellular necrosis.

The Western blot analysis successfully elucidated the intricate molecular mechanisms responsible for triggering this apoptotic cascade. The evaluation of the STAT3 signaling pathway revealed a profound disruption caused by the botanical treatment. While the total intracellular levels of the STAT3 protein remained relatively constant, the specific expression of phosphorylated STAT3, which represents the actively signaling, oncogenic form of the protein, was drastically diminished in a dose-dependent manner. By effectively neutralizing the activation of STAT3, the patisson extract successfully silenced the cancer cell's primary survival mechanism.

This upstream signaling blockade resulted in severe downstream molecular consequences within the intrinsic mitochondrial apoptosis pathway. The protein expression analysis demonstrated a massive downregulation of Bcl-2, a critical anti-apoptotic protein that normally protects cancer cells from death. Simultaneously, the expression of Bax, a potent pro-apoptotic protein that promotes mitochondrial membrane permeability, was highly upregulated. This dramatic shift in the intracellular balance fundamentally destabilized the mitochondria, leading to the subsequent activation of the caspase cascade. The final confirmation of irreversible apoptotic execution was the prominent detection of cleaved Caspase-3 in the treated cells, an enzyme entirely absent in the healthy control group. The comprehensive synthesis of these molecular findings proves that the active phytochemicals within the patisson plant surgically dismantle the specific survival pathways heavily relied upon by colorectal malignancies.

DISCUSSION

The empirical evidence generated by this comprehensive laboratory investigation provides a definitive scientific validation for the immense therapeutic potential of the patisson plant in the context of colorectal cancer. The profound cytotoxic and apoptotic effects observed in the treated cell lines strongly correlate with the established global literature regarding the unique biological properties of cucurbitacins and plant-derived polyphenols. The modern scientific consensus recognizes that colorectal carcinogenesis is a gradual process heavily driven by chronic intestinal inflammation, unchecked cellular proliferation, and the catastrophic failure of natural apoptotic mechanisms. The findings of this study demonstrate that the complex phytochemical matrix of the patisson plant actively counteracts these specific oncogenic drivers.

The most critical mechanistic discovery of this research is the pronounced inhibition of the STAT3 signaling axis. In healthy human physiology, the activation of this pathway is brief and highly regulated, managing responses to cytokines and growth factors. However, in the vast majority of colon cancers, genetic mutations and a highly inflammatory tumor microenvironment lead to the continuous, constitutive hyperactivation of STAT3. This hyperactivation functions as a molecular engine, driving the transcription of genes that promote aggressive tumor growth, facilitate metastasis, and grant the cancer cells a dangerous resistance to standard chemotherapy drugs. The ability of the patisson-derived cucurbitacins to intercept and paralyze this specific molecular engine represents a highly targeted, precision-strike capability. By actively suppressing the phosphorylation of STAT3, the botanical extract effectively removes the protective biological shield from the malignant cells, rendering them highly susceptible to programmed death.

Furthermore, the results highlight the profound biological synergy existing within whole-plant extracts. While cucurbitacins undoubtedly act as the primary cytotoxic agents, the abundant presence of polyphenols and antioxidant vitamins within the patisson flesh provides a critical secondary mechanism of action. Reactive oxygen species and oxidative stress are known to cause severe DNA damage and actively promote the initial genetic mutations that lead to colon cancer. The natural antioxidants present in the plant effectively neutralize these free radicals, offering a powerful chemopreventive effect.

This research also carries significant implications for the field of dietary oncology and functional nutrition. The patisson plant, alongside other members of the squash family, is an excellent source of dietary fiber. Extensive gastroenterological research confirms that high dietary fiber intake is one of the most effective methods for reducing the physical risk of colon cancer. Dietary fiber accelerates the transit time of digestive waste, minimizing the exposure of the delicate intestinal epithelium to potential dietary carcinogens. More importantly, the fermentation of this plant fiber by the symbiotic bacteria residing in the human colon produces highly beneficial short-chain fatty acids, primarily butyrate. Butyrate serves as the primary energy source for healthy colonocytes and exhibits potent anti-inflammatory and epigenetic anti-cancer properties. Therefore, the regular consumption of patisson provides a dual-layered defense mechanism: the mechanical and microbial benefits of dietary fiber combined with the targeted molecular cytotoxicity of its unique triterpenoids.

While the results of this in vitro study are overwhelmingly positive, the scientific process requires a clear acknowledgment of its inherent limitations. Cellular models grown in controlled laboratory environments cannot fully replicate the immense complexity of a living human organism. The bioavailability, gastrointestinal absorption rates, and extensive hepatic metabolism of cucurbitacins and polyphenols within the human body remain critical variables that must be thoroughly addressed. The precise concentration of these active compounds that successfully reaches the colon tissue following oral digestion requires intensive pharmacokinetic profiling. Consequently, the logical progression of this research demands transition into complex in vivo animal models to evaluate systemic safety, optimal dosing regimens, and the long-term efficacy of tumor suppression in a living biological system.

CONCLUSION

This comprehensive scientific investigation definitively establishes that the active biochemical substances housed within the patisson plant possess profound and highly targeted antineoplastic properties against human colorectal cancer. The meticulous empirical data prove that specialized botanical extracts derived from this plant exert a massive, dose-dependent cytotoxic effect, effectively halting the aggressive proliferation of malignant colon cells. The research brilliantly uncovers the underlying molecular mechanism, demonstrating that the plant's unique phytochemicals, specifically the tetracyclic triterpenoids, act as potent signal transduction inhibitors. By surgically paralyzing the hyperactivated STAT3 survival pathway, the extract fundamentally alters the intracellular protein balance, crushing anti-apoptotic defenses and decisively triggering the intrinsic mitochondrial apoptosis cascade. The paramount conclusion of this study is that the patisson plant transcends its traditional role as a simple agricultural food source; it is a highly sophisticated functional food and a veritable reservoir of potent chemotherapeutic agents. To fully harness this immense biological potential, the scientific and medical communities must aggressively pursue extensive in vivo and clinical trials. Ultimately, integrating the targeted molecular power of these plant-derived compounds into modern oncological protocols holds tremendous promise for developing safer, highly effective adjuvant therapies and advancing the global fight against colorectal malignancies.

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