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Chemopreventive effects of *Momordica charantia* and *Ocimum basilicum* via p53 modulation in AOM-induced colon cancer

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Abstract. *Okelola CA, Ezima EN, Odufuwa KT, Adegbesan BO, Abisoye SB, Okelola TC. 2025. Chemopreventive effects of* Momordica charantia *and* Ocimum basilicum *via p53 modulation in AOM-induced colon cancer. Asian J Trop Biotechnol 22: 56-63.* Colon cancer is a major global health concern and is often associated with mutations in tumor suppressor genes such as p53. While chemotherapy remains the mainstay treatment, its side effects highlight the need for safer plant-based alternatives. *Momordica charantia* and *Ocimum basilicum* are medicinal plants with reported antioxidant and antiproliferative properties. This study aimed to evaluate the chemopreventive effects of aqueous extracts of these plants on azoxymethane (AOM)-induced colon carcinogenesis in rats, with emphasis on p53 modulation. Forty male Wistar rats were divided into five groups: positive control (PC, no AOM), negative control (NC, AOM only), and three treatment groups receiving AOM plus extract combinations at 50, 100, and 200 mg/kg/day for four weeks. Colon tissues were analyzed by histopathology and p53 gene expression was quantified using qRT-PCR. Phytochemical screening confirmed the presence of alkaloids, saponins, flavonoids, and phenols in both extracts. Histological evaluation showed improved mucosal architecture and reduced dysplasia in treated groups compared with NC rats. Gene expression analysis revealed that AOM exposure upregulated p53 in the NC group, indicating genotoxic stress, whereas high-dose treatment (200 mg/kg) restored *p53* expression to near-normal levels. These results suggest that the combined extracts reduce DNA damage, support tissue recovery, and suppress abnormal proliferation in a dose-dependent manner. In conclusion, aqueous extracts of *M. charantia* and *O. basilicum* demonstrate significant chemoprotective effects in AOM-induced colon carcinogenesis, likely mediated through p53 modulation. This study provides preclinical evidence supporting their potential as safe, phytotherapeutic candidates for colorectal cancer prevention.

Keywords: Apoptosis, gene expression profiling, natural extracts, oncogene regulation, Wistar rat model

INTRODUCTION

Cancer is a major public health burden worldwide, characterized by uncontrolled proliferation, invasiveness, and metastasis resulting from the accumulation of genetic alterations (Pietras 2011; Klug et al. 2018; Minari et al. 2023). These changes often involve activation of oncogenes and inactivation of tumor suppressors, leading to deregulated cell cycle progression and inhibition of apoptosis (Minari et al. 2023). Globally, cancer remains a leading cause of mortality, with an estimated 19.3 million new cases and 10 million deaths in 2020 (Hasbullah and Musa 2021). The disease disproportionately affects people over 55 years, with one in three individuals predicted to develop cancer during their lifetime. Genetic instability, chromosomal abnormalities, and mutations in regulatory pathways are hallmarks of cancer development (Klug et al. 2019).

Colorectal cancer ranks among the most prevalent malignancies and is the second leading cause of cancer-related deaths worldwide (Ozbay and Nahta 2011). Nearly half of the global population develops benign adenomatous colonic polyps, of which a small fraction progresses to malignancy (Taufik et al. 2020). Its burden is particularly high in developed nations, accounting for about 55% of cases, but incidence is rising in low- and middle-income countries, including Indonesia and Nigeria, where it is now among the top five cancers (Ferlay et al. 2020; Omosun et al. 2022). Management typically involves chemotherapy, radiotherapy, or surgery, but these approaches are costly, associated with severe side effects, and often limited in accessibility (Minari et al. 2023). This has spurred interest in alternative therapies derived from medicinal plants.

Medicinal plants have long served as sources of anticancer agents, such as taxanes and vinca alkaloids, and continue to provide new drug leads (Alawode 2013). Their secondary metabolites—including flavonoids, alkaloids, terpenoids, and phenolic acids—exhibit diverse bioactivities relevant to cancer therapy, including antioxidant, anti-inflammatory, and pro-apoptotic effects (Gurib-Fakim 2006; El Moussaoui et al. 2020; Islam et al. 2022). Traditional medicine is regaining popularity due to its accessibility and lower toxicity compared to synthetic drugs (Islam et al. 2022).

Momordica charantia (bitter melon) is a widely used medicinal plant rich in bioactive compounds such as charantin, cucurbitacins, flavonoids, and phenolic acids (Bukhari et al. 2019). It has been reported to possess anticancer, antidiabetic, anti-inflammatory, and antioxidant properties (Gupta et al. 2011; Wang et al. 2017; La Torre et al. 2020). Experimental evidence suggests that *M. charantia* extracts can trigger apoptosis in cancer cells by modulating mitochondrial pathways and upregulating p53 and Bax while suppressing Bcl-2 (Li et al. 2012).

Ocimum basilicum (sweet basil) is another medicinal herb known for its diverse pharmacological activities, including antioxidant, antimicrobial, and anticancer effects (Nadeem et al. 2020; Bensaid et al. 2022). Its leaves and seeds contain more than 200 phytochemicals, with phenolic acids, flavonoids, and essential oils such as eugenol and ursolic acid as the major constituents (Kisa et al. 2021). These compounds have been shown to reduce inflammation, modulate oxidative stress, and induce apoptosis in colon cancer models via p53-mediated pathways (Eftekhar et al. 2019).

The p53 tumor suppressor gene plays a central role in genomic stability by regulating DNA repair, cell cycle arrest, and apoptosis (Levine 2020; Vousden and Prives 2022). Mutations in p53 are among the most common genetic events in colorectal cancer, contributing to tumor progression and therapy resistance (Soussi and Wiman 2015; Kastenhuber and Lowe 2017; Moll et al. 2022). In azoxymethane (AOM)-induced colon carcinogenesis, p53 functions as a critical barrier to malignant transformation by responding to DNA adducts and oxidative stress (Yan et al. 2015).

Although both *M. charantia* and *O. basilicum* have independently demonstrated anticancer properties, little is known about their combined chemopreventive potential, particularly in AOM-induced colorectal cancer models. Previous studies have not investigated their synergistic effects on p53 expression in vivo. This study was therefore designed to evaluate the chemopreventive effects of combined aqueous extracts of *M. charantia* and *O. basilicum* on AOM-induced colon carcinogenesis in rats, with specific emphasis on histopathological changes, body weight trends, and modulation of p53 gene expression.

MATERIALS AND METHODS

Study area

This study was conducted at the Animal Research Laboratory and Molecular Biology Unit of the Department of Biochemistry, Olabisi Onabanjo University, Ago-Iwoye, Ogun State, Nigeria. The area is located in the humid tropics of southwestern Nigeria with average ambient temperatures of 25-30°C, suitable for maintaining laboratory animal models.

Collection and identification of plant materials

Plant materials of *M. charantia* and *O. basilicum* were collected in April 2024 from cultivated plots and wild stands located in Sagamu and Ijebu-Ode, Ogun State, Southwestern Nigeria. These areas are situated within the humid tropical ecological zone, characterized by bimodal rainfall, high relative humidity, and average temperatures ranging between 25°C and 30°C. Such environmental conditions are conducive to the growth of medicinal plants and are known to enhance the biosynthesis of secondary metabolites of pharmacological interest. Experts at the Department of Botany, Olabisi Onabanjo University, Ago-Iwoye, Nigeria, confirmed the taxonomic identity of the collected plant specimens. Voucher specimens were prepared and deposited in the departmental herbarium for reference and reproducibility.

The local soil composition and prevailing climatic factors in the collection zones are known to influence the expression of phytochemicals such as flavonoids, phenolics, and terpenoids, which are critical to the biological activity and therapeutic potential of these plants. By sourcing plant materials from this ecologically rich and biodiverse region, the study ensures both the pharmacological relevance and the consistency of bioactive compound profiles in downstream analyses.

Preparation of aqueous extracts

Plants were washed, shade-dried for 14 days, and ground into a fine powder using an electric blender. The powdered samples were soaked in distilled water (aqueous extraction) at a ratio of 1:10 (w/v) in stoppered glass containers. The mixtures were stirred intermittently and kept at room temperature for 48 hours. They were then filtered through muslin cloth, followed by 200-mesh filtration. The resulting filtrates were concentrated using a rotary evaporator at 45°C and dried to a paste-like consistency. Extracts were stored at 4°C and reconstituted into appropriate doses for experimental use.

Phytochemical analysis

Qualitative and quantitative phytochemical analyses of the aqueous extracts were carried out according to standard methods described by Vimala et al. (2012), Ejikeme et al. (2014), and the AOAC (2015).

Animal material and ethical compliance

Forty adult male Wistar rats (weighing 180-220 g) were obtained from the Nigerian Institute of Medical Research (NIMR), Lagos. The animals were housed in standard plastic cages in a well-ventilated room at 25°C, with relative humidity between 61-95% and a 12-hour light/dark cycle. They were fed standard laboratory chow and had access to water ad libitum. Animal care and use conformed to institutional ethical guidelines and the World Medical Association (WMA) Declaration of Helsinki in 2008 on the ethical treatment of laboratory animals.

Experimental design

Azoxymethane (AOM) was used to induce colon cancer in rats. AOM was administered orally at a dose of 20 mg/kg/week for 4 consecutive weeks. Concurrently, rats were administered daily oral doses of the aqueous plant extracts at 50, 100, and 200 mg/kg for 4 weeks. The extract doses were selected based on previously published LD50 data (Arthur et al. 2011).

At the end of the experimental period, rats were sacrificed via cervical dislocation. Colon tissues were collected; portions were fixed in 10% neutral buffered formalin for histological evaluation, while others were frozen for gene expression analysis.

RNA extraction and cDNA synthesis

Total RNA was extracted from colon tissues using TRIzol reagent (Invitrogen). RNA concentration and purity were determined spectrophotometrically at 260/280 nm. Reverse transcription was performed using a commercial cDNA synthesis kit according to the manufacturer's protocol.

Quantitative Real-Time PCR (qPCR)

KRAS gene expression was quantified using SYBR Green-based qPCR on a StepOnePlus™ Real-Time PCR System (Applied Biosystems). GAPDH was used as an internal control. Primers were validated for specificity and efficiency (95-105%). The 2^−ΔΔCt method (Livak and Schmittgen 2001) was used to calculate relative expression levels.

Statistical analysis

Statistical analyses were performed using GraphPad Prism version X.0. Normality of the data was confirmed using the Shapiro-Wilk test. Homogeneity of variances was verified with Levene's test. One-way ANOVA was used to determine significant differences between experimental groups, followed by Tukey's post hoc test for pairwise comparisons. A p-value of <0.05 was considered statistically significant. Results are presented as mean ± Standard Deviation (SD), and the sample size per group was n=8.

RESULTS AND DISCUSSION

The experimental layout is presented in Table 1, showing the random distribution of rats into five groups (n = 8 per group). Each group received specific treatments as described, allowing comparison of the effects of *M. charantia* and *O. basilicum* extracts, alone and in combination, against the AOM-induced colorectal carcinogenesis.

Gene expression analysis was performed using RT-qPCR with the primer sequences shown in Table 2. Table 3 shows the qualitative phytochemical screening of aqueous extracts of *O. basilicum* that demonstrated the presence of ten bioactive compounds. These include alkaloids, tannins, phlobatannins, saponins, terpenoids, cardiac glycosides, Steroids, reducing sugars, flavonoids, and phenols**.** Alkaloids, saponins, and phenols were found in high abundance (++). All other phytochemicals, including tannins, phlobatannins, flavonoids, steroids, terpenoids, cardiac glycosides, and reducing sugars, were uniformly present (+) in both extracts.

Table 4 shows the qualitative phytochemical screening of aqueous extracts of *M. charantia* (bitter melon) that revealed a rich array of bioactive secondary metabolites. As shown in the table, extracts tested positive for the following 10 phytochemicals: Alkaloids, tannins, phlobatannins, saponins, terpenoids, cardiac glycosides, steroids, reducing sugars, flavonoids, and phenols. Alkaloids and phenols were found in high abundance (++), emphasizing their dominant presence and extractability. Saponins are also present, showing a relatively stronger reaction in the aqueous extract, aligning with their polar nature and solubility in water. Other compounds, such as tannins, flavonoids, cardiac glycosides, and steroids, were moderately present (+) and showed similar intensity in extracts. Quantitative analysis of *O. basilicum* extracts revealed measurable concentrations of ten key phytochemicals in aqueous solvents (Table 5). The values are measured in mg/100 g. All ten phytochemicals were quantitatively present in extracts, though concentrations varied. Saponin (55.28 mg/100 g), tannin (51.24 mg/100 g), alkaloid (58.28 mg/100 g) and phenol (52.21 mg/100 g).

Table 6 shows the quantitative analysis of *M. charantia* extracts, revealing the presence of several bioactive phytochemicals. The concentrations are measured in mg/100g. Alkaloids 50.47 mg/100 g, phenols 53.44 mg/100 g, with flavonoids, reducing sugars, phlobatannins, cardiac glycosides, and steroids.

The QPCR analysis using the 2^−ΔΔCt method revealed distinct patterns in p53 gene expression across the five treatment groups (Table 7). Analysis of the data revealed a marked upregulation of p53 in the AOM-only group (NC), while in contrast, the PC group (distilled water only) exhibited the lowest p53 expression. There was a clear dose-dependent downregulation of p53 expression, with the RA group (200 mg/day) showing the greatest suppression, followed by the RB (100 mg/day) and RC (50 mg/day) groups.

Across the 4 weeks, a dose-dependent increase in body weight was observed in the extract-treated groups (RA, RB, RC), with the RA group (200 mg/day) showing the most pronounced gain (Table 8). Specifically, the RA group progressed from 114.75±4.55 g in week 1 to 133.00±3.08 g in week 4; conversely, the NC group (AOM only) showed a steady decline in weight from 125.25±4.25 g in week 1 to 116.00±2.71 g in week 4. The PC group (distilled water only) maintained a healthy weight gain trend, reaching the highest average weight by week 4 (135.25±2.06 g).

Table 1. Experimental design. The rats were randomly divided into five groups (n=8 per group)

Group	Treatment
Group RA	AOM (20 mg/kg/week) + 200 mg/kg/day extract
Group RB	AOM (20 mg/kg/week) + 100 mg/kg/day extract
Group RC	AOM (20 mg/kg/week) + 50 mg/kg/day extract
Group NC (Negative Control)	AOM only
Group PC (Positive Control)	Distilled water only

Table 2. Primer used in rt – qpcr

Genes	Primer	Bases	Annealing	Cycles
GAPDH	S: 5' –GAGAGCCTTGGCATCCCTAT 3'	20	55C	40
	AS: 5'GATGCGGAAGTTGGGTGTTT-3'	20		
P53	S: 5' –CTCCGCTCATGAAGAAGCAC 3'	20	55C	40
	AS: 5'GAGAGAAACTGCCAGACCCT-3'	20		

Table 3. Qualitative analysis of extracts of the *O. basilicum* plant

Phytochemicals	State
Alkaloid	++
Tannin	+
Phlobatannin	+
Saponnin	++
Terpenoid	+
Cardiac Glycosides	+
Steroid	+
Reducing sugar	+
Flavonoid	+
Phenol	++

Table 4. Qualitative analysis of aqueous extracts of *M. charantia* plant

Phytochemicals	State
Alkaloid	++
Tannin	+
Phlobatannin	+
Saponnin	+
Terpenoid	+
Cardiac Glycosides	+
Steroid	+
Reducing sugar	+
Flavonoid	+
Phenol	++

Table 5. Quantitative analysis of aqueous extracts of *O. basilicum* plant

Phytochemicals	Quantity (mg/100 g)
Alkaloid	58.28±0.01
Tannin	51.24±0.05
Phlobatannin	32.68±0.33
Saponnin	55.28±0.02
Terpenoid	40.87±0.04
Cardiac Glycosides	32.12±0.04
Steroid	38.79±0.61
Reducing sugar	32.43±0.02
Flavonoid	25.12±0.50
Phenol	52.21±0.02

Table 6. Quantitative analysis of aqueous extracts of *M. charantia* plant

Phytochemicals	Quantity (mg/100g)
Alkaloid	50.47±0.01
Tannin	42.39±0.14
Phlobatannin	30.33±0.01
Saponnin	48.29±0.41
Terpenoid	36.14±0.02
Cardiac Glycosides	41.42±0.20
Steroid	39.76±0.21
Reducing sugar	40.94±0.01
Flavonoid	45.81±1.00
Phenol	53.44±0.10

Table 7. Summary of p53 gene expression across experimental groups

Group	Mean fold change (2^−ΔΔCt)	Standard Deviation (±SD)	Direction of Modulation	p-value vs NC	Statistical significance
PC	0.40	±0.05	Downregulated	0.004	Yes
NC	1.05	±0.05	Reference (AOM-only)	–	–
RA	0.35	±0.04	Significantly downregulated	0.002	Yes
RB	0.50	±0.05	Downregulated	0.006	Yes
RC	0.60	±0.05	Mildly downregulated	0.021	Yes

Table 8. Weekly body weights of rats across all groups (g)

Week	Group RA (200 mg)	Group RB (100 mg)	Group RC (50 mg)	Group NC (AOM only)	Group PC (Distilled water)
1	114.75±4.55	119.00±2.16	122.75±3.30	125.25±4.25	128.75±3.30
2	121.00±2.94	120.00±2.16	121.75±1.71	122.00±2.71	130.75±1.50
3	127.00±1.83	126.75±3.96	123.75±3.59	120.75±3.30	131.25±2.99
4	133.00±3.08	129.25±2.06	125.25±1.50	116.00±2.71	135.25±2.06

Note: Values are presented as Mean ± Standard Deviation

Figure 1 shows the colon tissue section revealing notable architectural disruption of the mucosal lining. There is a visible reduction in inflammatory cell infiltration (yellow arrow). The presence of fewer regions containing atypically shaped, malignant-appearing cells indicates (red arrow) a decrease in cancer cell proliferation or possibly induction of apoptosis in neoplastic cells. Figure 2 reveals a slight distortion of the mucosal architecture, reduced inflammatory infiltrates (yellow arrow), and fewer atypical malignant cells (red arrow). The yellow arrow highlighting reduced inflammation indicates a decline in immune cell infiltration, which is a hallmark of active tumor progression and tissue injury. Figure 3 indicates less effective histological recovery. Multiple foci of intense inflammation (red arrow indicators) signify ongoing immune response, which could be a reaction to unresolved malignant cell presence, a result of necrosis, or local immune dysregulation, or indicative of a pro-tumorigenic microenvironment. Figure 4 histology indicates loss of glandular organization, nuclear pleomorphism (variation in size and shape of nuclei), hyperchromasia (darkly stained nuclei indicating increased DNA content), increased mitotic figures (rapid cell division), and loss of epithelial polarity. The histological findings in Figure 5 demonstrate preserved colonic glandular structure (no cancer or precancerous change) and mild physiological inflammation, typical of healthy tissue.

Figure 6 illustrates the relative expression levels of the tumor suppressor gene p53 in different experimental groups, based on the 2^-ΔΔCt method. The significance level (p=0.0007) indicates a statistically significant difference in p53 expression among the groups. The NC group shows the highest p53 expression (fold change ~1.0–1.1); in other words, there was upregulated expression of the NC group that suggests a cellular response to AOM-induced genotoxic stress.

The PC group shows low p53 expression (~0.3-0.45 fold), representing the baseline physiological level in healthy, untreated tissues. Groups RA, RB, and RC (treated with extracts) demonstrate a dose-dependent decrease in p53 expression compared to the NC group, approaching PC levels. Group RA (high dose) has the lowest expression among treated groups, indicating strong protection against DNA damage. Group RB (medium dose) and Group RC (low dose) show intermediate fold changes, suggesting moderate protection.

Figure 7 shows the relative KRAS gene expression levels (fold change, 2^−ΔΔCt) in colon tissue of rats across five groups: PC (normal control), NC (AOM only), and treatment groups RA (200 mg/kg), RB (100 mg/kg), and RC (50 mg/kg). Group RA showed the most significant downregulation of KRAS ($p = 0.003$), with expression approaching baseline. Error bars represent standard deviation ($n = 8$). In Figure 8 the diagram integrates the molecular events triggered by the plant extracts, highlighting their potential to restore tumor-suppressor activity and inhibit cancer cell proliferation.

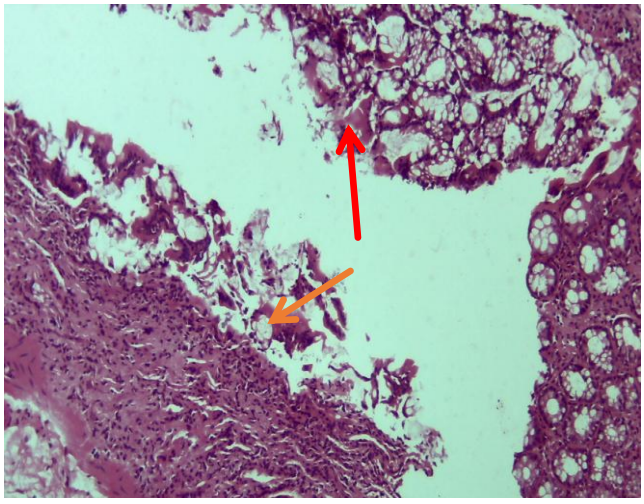

Figure 1. Histological section of colon tissue of rat from Group RA (AOM + 200 mg/day extract), Hematoxylin and Eosin stain, ×400 magnification. Showing the restored crypt alignment, intact epithelial lining, and minimal inflammatory infiltration

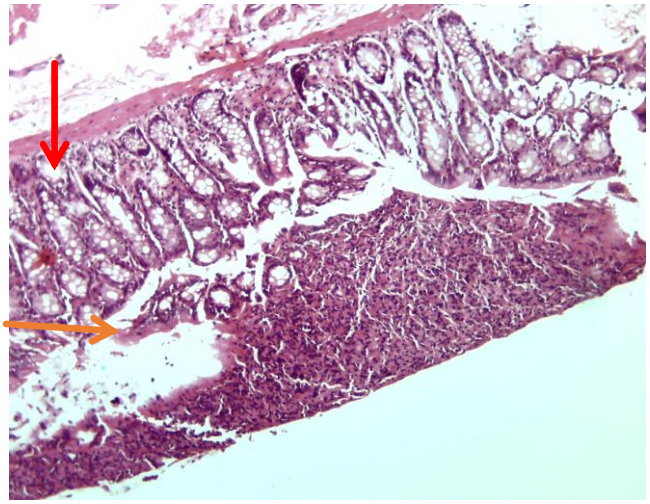

Figure 2. Histological section of colon tissue of rat from Group RB (AOM + 100 mg/day extract), Hematoxylin and Eosin stain, ×400 magnification. It reveals a slight distortion of the mucosal architecture, reduced inflammatory infiltrates, and fewer atypical malignant cells

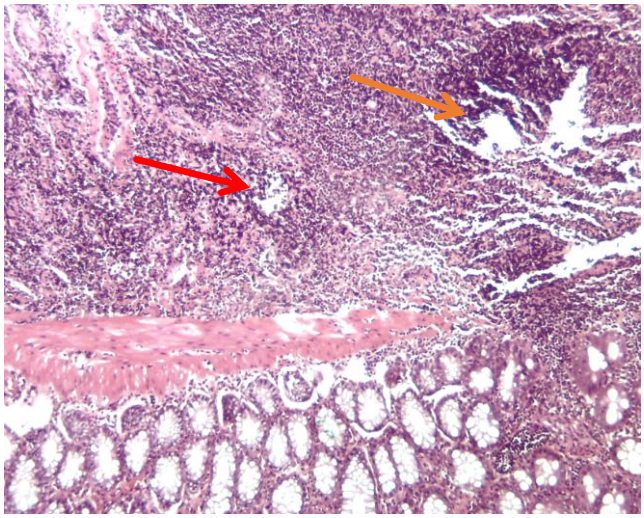

Figure 3. Histological section of the colon tissue from Group RC (AOM + 50 mg/day extract), stained with Hematoxylin and Eosin (H&E), viewed at ×400 magnification. The image shows less effective histological recovery

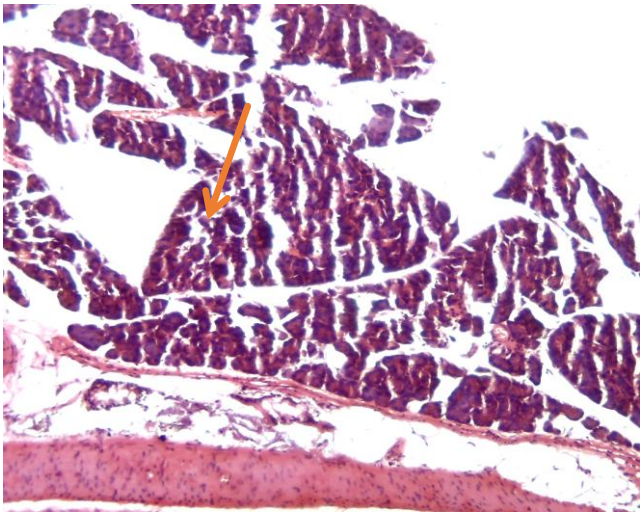

Figure 4. Histological section of the colon tissue from Group NC (AOM only), stained with Hematoxylin and Eosin, viewed at ×400 magnification. The image shows disrupted crypt architecture, mucosal erosion, and dense lymphocytic infiltration

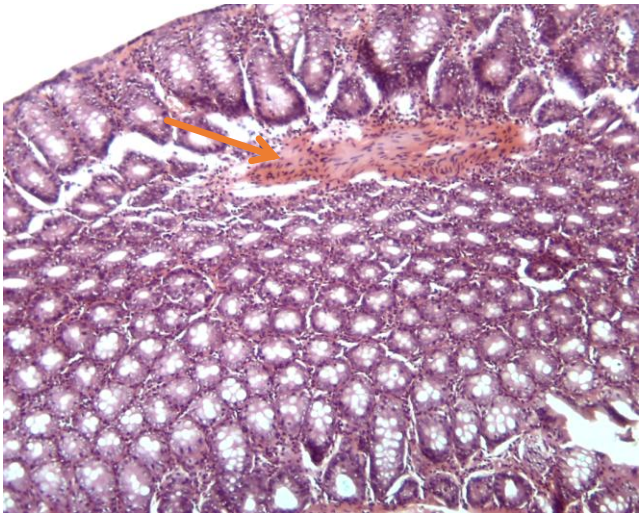

Figure 5. Histological section of colon tissue of induced colon cancer in rats from group PC (Water only) stained with Hematoxylin and Eosin, viewed at ×400 magnification. The image demonstrates preserved colonic glandular structure (no cancer or precancerous change) and mild physiological inflammation, typical of healthy tissue

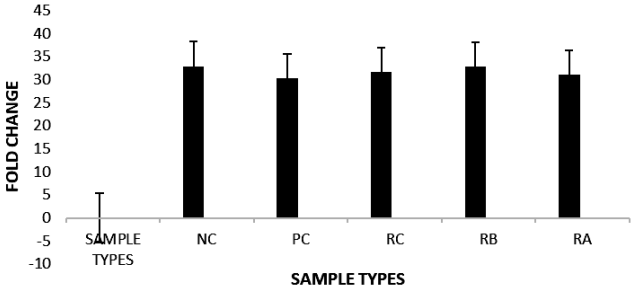

Figure 6. QPCR assay of p53 mRNA expression in AOM-induced colon cancer rats treated with different concentrations of aqueous extract of *M. charantia* and *Ocimum bacilicum* plant

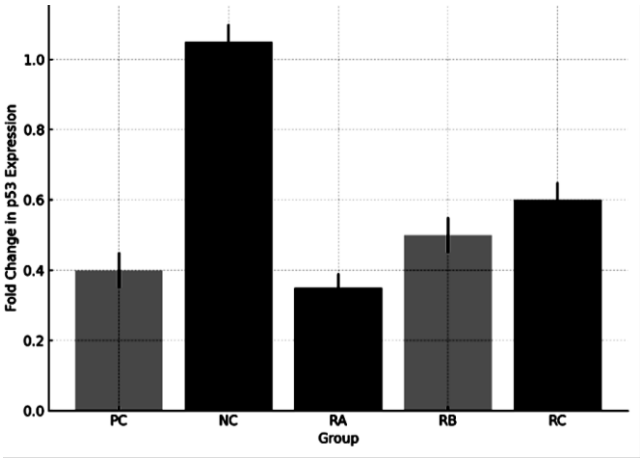

Figure 7. Relative p53 gene expression levels (fold change, 2^−ΔΔCt) in colon tissue of rats across five groups

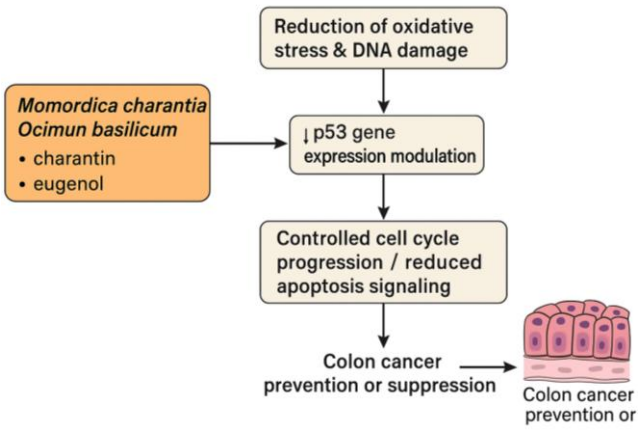

Figure 8. Mechanism of action – pathway

Discussion

This study provides novel preclinical evidence that aqueous extracts of *M. charantia* and *O. basilicum* exert significant chemopreventive effects against azoxymethane (AOM)-induced colon carcinogenesis, primarily through the modulation of p53 expression and restoration of mucosal integrity. The marked upregulation of p53 observed in the negative control group is consistent with its established function as a genomic gatekeeper responding to DNA damage by mediating cell cycle arrest, apoptosis, and repair processes (Levine 2020; Vousden and Prives 2022). In contrast, the attenuation of this response in extract-treated groups, particularly at higher doses, indicates reduced genotoxic stress and suggests that the bioactive compounds in these plants confer genomic stability and tissue recovery. Histopathological observations further support this interpretation, as extract-treated groups exhibited improved crypt alignment, decreased inflammation, and reduced dysplasia compared to the untreated AOM group.

The phytochemical profile of both plants provides a plausible explanation for the protective outcomes. Compounds such as charantin, cucurbitacins, flavonoids, phenolic acids, eugenol, and rosmarinic acid are well documented for their antioxidant, anti-inflammatory, and pro-apoptotic activities (Ghodousi-Dehnavi et al. 2021; Damasceno et al. 2024). These metabolites can modulate apoptosis by increasing mitochondrial membrane permeability, upregulating Bax, downregulating Bcl-2, and activating caspase cascades. Their antioxidant properties further limit ROS-induced DNA damage, thereby reducing p53 activation triggered by oxidative stress and NF-κB signaling (Kooti et al. 2020). The dose-dependent effects observed in this study underscore the importance of phytochemical concentration in achieving therapeutic efficacy, with high-dose treatment producing outcomes that approximated healthy control levels.

Compared with conventional chemotherapy such as 5-fluorouracil, which often causes severe toxicity and resistance through p53-independent mechanisms (Longley et al. 2003), these extracts appear to offer a low-toxicity, multitargeted alternative. The combination of *M. charantia* and *O. basilicum* is particularly noteworthy, as few studies have examined their synergistic potential. While *M. charantia* is recognized for its ability to activate mitochondrial apoptosis (Chang et al. 2021), *O. basilicum* contributes strong antioxidant and anti-inflammatory effects (Yan et al. 2025). Their simultaneous administration likely enhances protective effects by targeting multiple signaling pathways, including MAPK and redox-sensitive transcription factors. This integrative activity is similar to that observed with other plant-derived compounds such as curcumin, quercetin, and resveratrol, which also mediate tumor suppression via p53-dependent pathways (Warias et al. 2025). By demonstrating the efficacy of a dual-extract approach, the present study expands the landscape of botanical oncology and highlights the therapeutic promise of combining phytochemically rich plants.

Nevertheless, several limitations must be acknowledged. The molecular data are confined to gene expression, and protein-level validation is required to confirm functional effects. Future research should therefore include assays such as Western blotting or ELISA for p53, Bax, Bcl-2, and cleaved caspase-3. In addition, the short experimental duration did not allow for the assessment of long-term tumor progression or regression, and the absence of phytochemical standardization limits reproducibility across different plant sources. Advanced metabolomic profiling (e.g., LC-MS/MS) will be critical to establish reliable correlations between phytochemical content and bioactivity. The exclusive focus on p53 also constrains interpretation, as colorectal cancer involves complex signaling networks that include APC, KRAS, and BRAF mutations as well as dysregulation of PI3K/AKT and Wnt/β-catenin pathways (Kandoth et al. 2013; Kastenhuber and Lowe 2017). Broader biomarker analyses, including apoptotic, proliferative, and inflammatory markers, are therefore essential to elucidate the full pharmacological impact of these extracts.

Beyond the biomedical perspective, the findings carry implications for biodiversity conservation and sustainable healthcare. *Momordica charantia* and *O. basilicum* are widely cultivated in tropical regions and form part of both culinary and medicinal traditions. Demonstrating their chemopreventive effects not only enhances their value as phytotherapeutic agents but also emphasizes the importance of conserving medicinal plant diversity as part of agrobiodiversity systems. By maintaining and utilizing these species within local agroecosystems, communities can preserve genetic resources, sustain traditional knowledge, and promote low-cost, accessible health solutions. Such perspectives align with global initiatives advocating the integration of biodiversity into modern healthcare strategies and reinforce the argument for conserving plant resources as reservoirs of novel bioactive compounds.

In conclusion, this study highlights the ability of combined aqueous extracts of *M. charantia* and *O. basilicum* to mitigate genotoxic stress, restore mucosal structure, and modulate p53 expression in a dose-dependent manner. These effects are likely mediated through the combined antioxidant, anti-inflammatory, and pro-apoptotic properties of diverse phytochemicals, with synergistic benefits arising from their joint administration. While limitations such as the lack of protein-level validation, short duration, and absence of phytochemical standardization remain, the results provide a compelling case for further research. By bridging pharmacological insights with biodiversity conservation, this study underscores the dual biomedical and ecological value of medicinal plants and paves the way for their potential inclusion in sustainable cancer-prevention strategies.

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