ABSTRACT

The Effect *Momordica Charantia* Extracts on a Precancerous Model of Colorectal Cancer

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Aberrant crypt foci (ACF) are possible precursors to colorectal cancer. It is therefore hypothesized that compounds which inhibit ACF formation have the potential to prevent colorectal cancer. Studies have shown that compounds extracted from turmeric, garlic, onion, green tea and other fruits and vegetables were able to inhibit ACF formation. In this study the chemopreventive activity of extracts of *Momordica charantia* against the formation of 1, 2 dimethylhydrazine (DMH)-induced ACF was investigated. The possible mode of action was also investigated.

To examine the inhibitory effect of *Momordica charantia* on DMH-induced ACF formation, male Sprague Dawley rats were randomly assigned to three groups. Group one (control) was given subcutaneous injection of 1,2 dimethylhydrazine only (40mg/Kg). Groups two and three received dimethylhydrazine (40mg/Kg) and *Momordica charantia* fruit and seed extract, respectively (60mg/Kg). After 12 weeks the animals were sacrificed using an over dose of Sodium pentobarbital. The colon was removed, stained in 1% methylene blue and viewed under a compound microscope. Aberrant crypt foci were scored for number, distribution pattern along the colon and crypt multiplicity. Selected ACF were resected for histological analysis.

The crude ethanolic extracts of the seed and fruit were further purified using liquid-liquid partition and Thin Layer Chromatography (TLC). Four fractions were obtained, and the seed fractions were selected and administered to male Sprague-Dawley rats. The rats were randomly assigned to five treatment groups. All groups received subcutaneous injections of 1,2 dimethylhydrazine. Group 1 (control) received dimethyl sulfoxide (DMSO), while groups 2,3,4 and 5 received hexane, chloroform, ethylacetate, and water fraction respectively for twelve weeks. Urine samples were collected at the beginning and end of the experimental period and 5-methyl-2-deoxy cytidine concentration was determined. The colons were also removed and examined grossly.

Treatment with *Momordica charantia* seed and fruit extract at a dose of 60mg/kg significantly inhibited the average colonic ACF formation ($p<0.05$). The seed

extract significantly inhibited ACF formation with two or more crypts per focus (≥2C/F). Overall most of the ACF were observed in the middle colon. Histological analysis of selected ACF revealed that most ACF were hyperplastic while some showed mild dysplastic change.

Of the four liquid-liquid partition fraction (20mg/Kg) only the chloroform and water fractions significantly inhibited the average colonic ACF formation ($p<0.05$). In terms of crypt multiplicity the chloroform fraction significantly inhibited ACF with a multiplicity of one, while the water fraction resulted in a significant reduction of ACF with a multiplicity of two ($p<0.05$). Most extracts except the ethyl acetate fraction produced a significant reduction of ACF in the proximal colon ($p<0.05$).

Since epigenetic changes such as DNA hypomethylation and hypermethylation are early events in colorectal cancer development, the effect of each fraction on 5-methyl-2-deoxy cytidine concentration was evaluated. The control group excreted elevated levels of 5-methyl-2-deoxy cytidine 19 hours after the final 1.2 dimethylhydrazine injection, while all the other groups except the group fed water extract excreted significantly less ($p<0.05$). By week 12 most groups excreted similar amount of 5-methyl-2-deoxy cytidine in their urine, except the hexane group which had a slight elevation.

These findings showed that extracts of *Momordica charantia* may inhibit ACF formation and may be a possible chemopreventive agent against colorectal cancer carcinogenesis. One possible mechanism by which it may inhibit ACF formation is by affecting DNA methylation patterns in other words preventing hypermethylation or hypomethylation of the DNA.

Keywords: Tamika Stacy-Ann Wynter; *Momordica Charantia*; DNA methylation; Aberrant Crypt foci; colorectal cancer