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## **Probiotics administration ameliorate azoxymethane induced-carcinogenesis by reducing the formation of aberrant crypt foci and modulation oxidative stress in rats**

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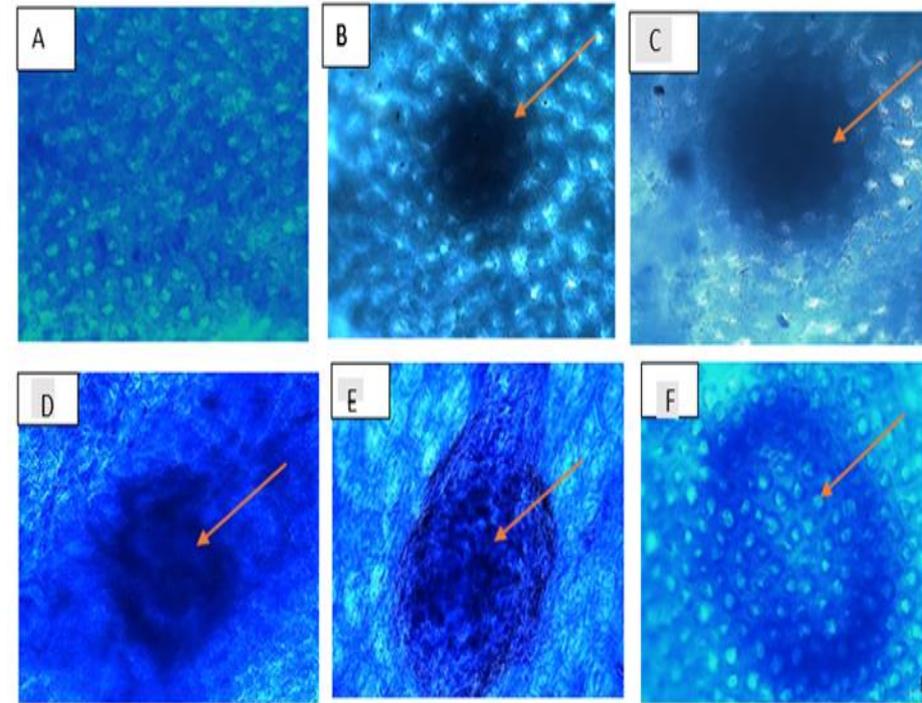
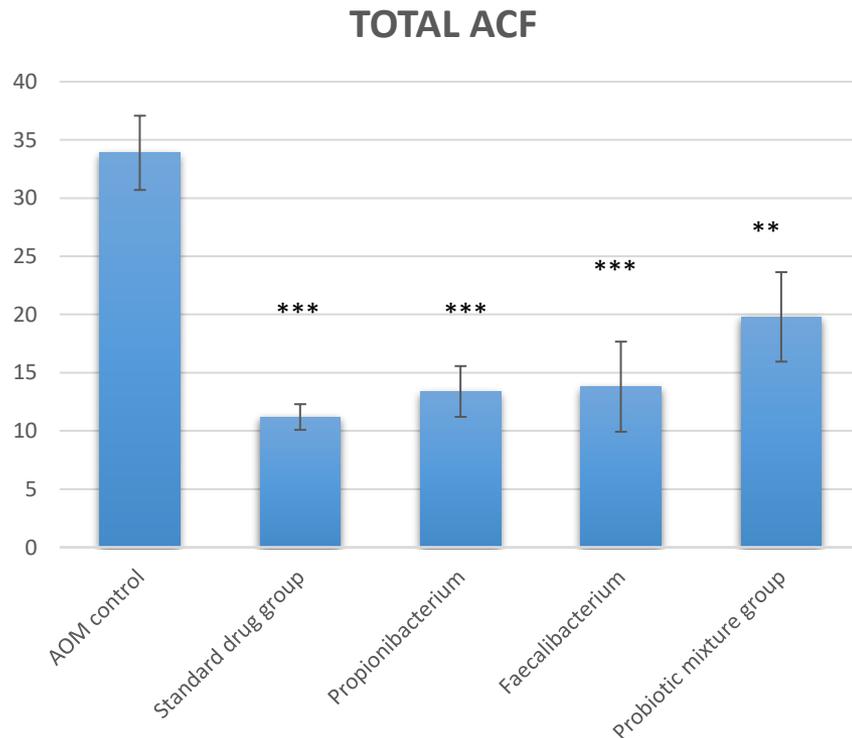


**Abstract:** Aberrant crypt foci (ACF) are early lesions in the neoplastic induction found in the rat colon of carcinogenic model. ACF are one of the first changes in the colon that lead to colorectal cancer (CRC). Probiotics and fermented foods are well known for their beneficial role in gut health and previous studies showed their therapeutic effects on gastrointestinal diseases. The aim of this study is to investigate the preventive role of *Propionibacterium freudenreichii* and *Faecalibacterium prausnitzii* probiotics against CRC in rats induced with azoxymethane (AOM). Microscopical examination of rat colons after methylene blue staining showed that the total number and multiplicity of ACF were significantly lower in the probiotic groups ( $p < 0.05$ ) than the AOM control group. Histological examination of the colon showed increased severe hyperplasia and dysplasia of the ACF in the AOM control group compared to the treatment groups. Probiotics administration also reduced the levels of malondialdehyde (MDA) in the colon of the rats compared to the rats in the AOM control group. These results suggest that probiotics play a preventive role in CRC initiation and development by slowing down ACF formation, reducing the severity of ACF lesions and reducing lipid peroxidation levels in the colon.

**Keywords:** Probiotics; Colorectal cancer; *Propionibacterium freudenreichii*; *Faecalibacterium prausnitzii*; Oxidative stress.

# Results and Discussion

## ACF Frequency and Microscopical findings



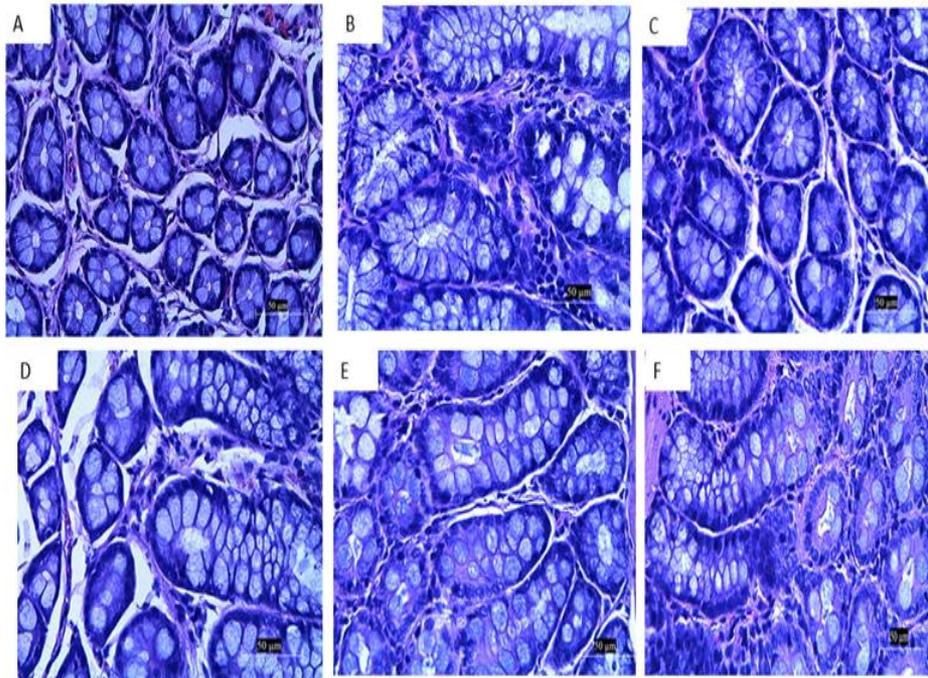
**Figure 2:** A topographic view shows the ACF found in the colon of the different groups. (A) Normal control group (B) AOM control group (C) Standard drug group (D) Propionibacterium group (E) Faecalibacterium group (F) Probiotics mixture group

**Figure 1:** Total ACF count for the different groups. Values were expressed as mean ± S.E.M, values with \* $p < 0.05$ , \*\* $p < 0.01$  and \*\*\* $p < 0.001$  are significant when compared to AOM group.

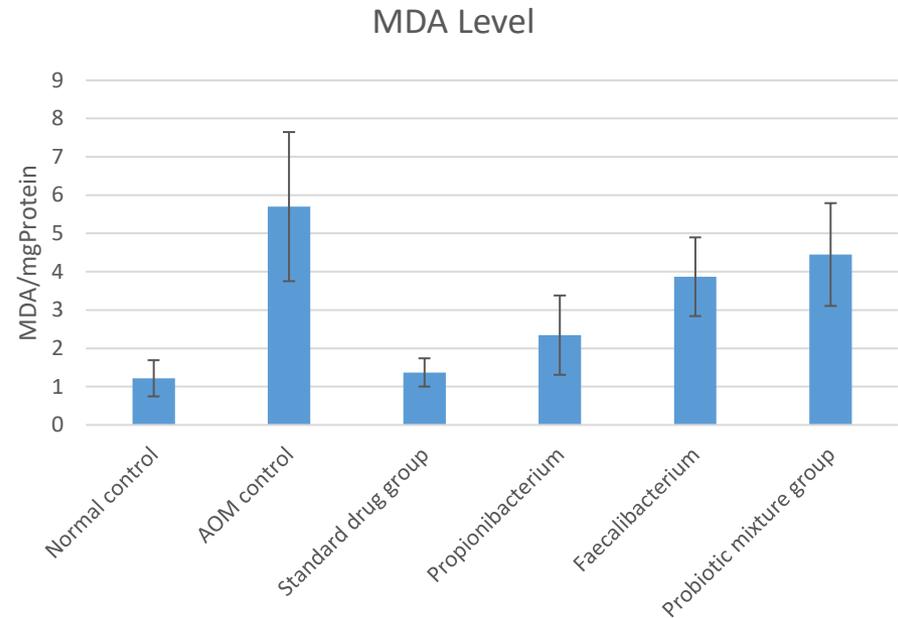
# Results and Discussion

## Probiotics administration reduced MDA levels

### Histological findings



**Figure 3:** A topographic view shows the ACF found in the colon of the different groups. (A) Normal control group (B) AOM control group (C) Standard drug group (D) Propionibacterium group (E) Faecalibacterium group (F) Probiotics mixture group



**Figure 4:** Lipid peroxidation level in treated and untreated groups. All values were expressed as mean  $\pm$ SEM

# Discussion

- The probiotic microorganisms were found to be effective in preventing the development of ACF and reducing the number of aberrant multi crypt and preneoplastic lesions in the rat colon in this study
- In AOM control group, the presence of overcrowding and elongation of the nuclei, atypical epithelial cells, and architectural atypia indicated that the majority of the ACF were dysplastic aberrant crypts, which are precursor lesions, however probiotics were able to reduce the number and multiplicity of ACF.
- MDA levels were lower in the probiotic groups than in the AOM control group, but the differences were not statistical significantly.

# Conclusion

- The findings from this study suggest that probiotics can help prevent CRC by slowing the progression of ACF, reducing the incidence of ACF lesions, and decreasing lipid peroxidation in the colon.
- Since the inhibition of ACF development in the mixture group was lower than in the two individual probiotic groups, we infer that there is no synergistic effect between *P. freundreichii* and *F. prausnitzii* against CRC.

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**Conflicts of Interest:** The authors declare no conflict of interest.

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