

Reduction in Colon Cancer Risk by Red Wheat Consumption

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Research Questions

Colon cancer is the third most common cancer in both men and women. We have recently accumulated results from several animal studies demonstrating that red wheat has a significant ability to reduce colon cancer risk. White wheat, depending on the marker of colon cancer risk used, had either less ability than red wheat or no ability to reduce cancer risk.

The overall objective of this proposal will be to determine the effect of feeding red wheat and white wheat on risk of colon cancer risk in an animal model, the carcinogen-treated rat. The specific aims will be as follows:

- 1) To confirm that red wheat reduces the number of pre-cancerous lesions that develop in the colon of carcinogen-treated rats, particularly in relation to white wheat.
- 2) To determine whether red wheat reduces the development of cancer stem cells in the colon of carcinogen-treated rats.

Results

The graduate student conducting the study has now acquired the skills that will be used in measuring the pre-cancerous lesions and has begun learning the immunohistochemical techniques that will be used in determining the number of cancer stem cells that develop. The 10 week animal feeding trial is concluding now, and tissues are being processed and sent to the histology laboratory for preparation for immunohistochemistry. Counting of pre-cancerous lesions will begin in the next 1-2 weeks. Immunohistochemical detection of cancer stem cells will begin in 4-6 weeks.

Application/Use

If our hypothesis is correct, that red wheat will reduce colonic pre-cancerous lesions and accumulation of cancer stem cells in the colon, this will provide much more convincing evidence that red wheat protects against colon cancer. This message can be used to promote red wheat consumption. Given that currently there is a growing movement promoting consumption of gluten-free (i.e. non-wheat containing) foods, this would provide a strong justification for including red wheat-containing products in the diet.

Material and Methods

We have administered a colon-specific carcinogen (dimethylhydrazine) to three groups of rats (12 per group) and then 4 days later begin feeding one of three diets, as follows: a wheat-free control diet, a diet containing 65% refined red wheat, and a diet containing 65% refined white wheat. After 10 weeks, the rat colons are removed and cleaned. One half the colon (split longitudinally) will be used for counting a common marker of early colon cancer risk, called aberrant crypt foci, under a light microscope by our usual procedure.

The other half will be processed for detection of a stem cell marker. This will be done by immunohistochemistry. Briefly, the colon will be fixed in formalin, embedded in paraffin, and cut into very thin sections (4 μm) *en face*, which will be mounted on glass slides. The sections on the slide will then be covered with a solution containing an antibody specific for the stem cell marker (called Lgr5), followed by another solution which will cause a color to develop wherever there is antibody bound to Lgr5. The amount of color is then measured under a light microscope using image analysis software. If red wheat decreases the amount of color, this indicates that it decreased the number of cancer stem cells that developed in the crypts.

Economic Benefit to a Typical 500 Acre Wheat Enterprise:

If our findings show a reduction in colon cancer risk in our animal model, as hypothesized, this can be used to promote red wheat consumption, and to offer a counter message to those promoting gluten-free diets. This could increase demand for red wheat, and thus potentially increase the price of red wheat.

Related Research

We are currently conducting studies examining the effect of vegetables on reducing risk of colon cancer, using a food-borne carcinogen that develops in well-done meat and fish. This carcinogen belongs to a group of compounds referred to as heterocyclic aromatic amines (HAA). Since HAA are present in the diet, they represent a more realistic carcinogen than the carcinogen used in our present project – dimethylhydrazine – which is not found in the diet. If our studies with HAA indicate that it is an appropriate carcinogen for use in studies of diet and colon cancer, we would consider using HAA as the colon carcinogen in future studies of the reduction in colon cancer risk with red wheat, in order to provide greater relevance to the studies.

Recommended Future Research

Unfortunately, human studies of reduction in risk in colon cancer are extremely expensive and difficult, and can only be done using very indirect, and therefore uncertain, markers. Thus, animal studies will continue to be the type of studies that will need to be done. Although most studies of colon cancer in animal models use a chemical carcinogen, such as we are doing, there are genetic models of colon cancer. To further establish the cancer-protecting effect of red wheat, a study using one of these genetic models of colon cancer could be used. Establishing a protective effect of red wheat against colon cancer in both chemically-induced colon cancer and genetically-induced colon cancer would be extremely powerful evidence that red wheat protects against colon cancer.