MRN-100 Exerts Anti-Cancer in the Gastroesophageal Tract

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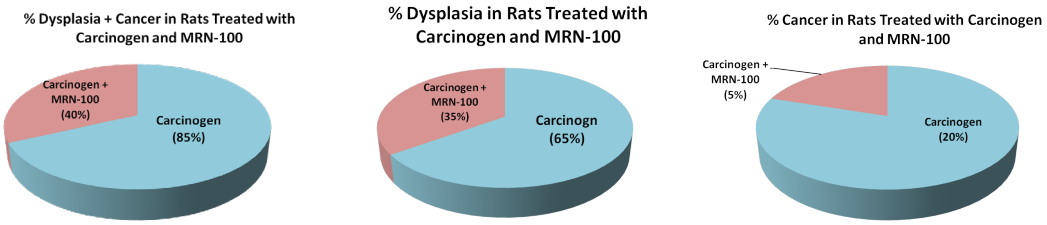
Gastric and esophageal cancers are two leading causes of cancer-related deaths throughout the world (1). The American Cancer Society estimates that in 2016 in the United States, ~16,900 new esophageal cancer cases will be diagnosed and about 15,700 deaths will occur from esophageal cancer (2). The estimates for stomach cancer diagnoses are about 26,400 cases and about 10,700 people will die from this type of cancer (3). Additionally, Japan has the third highest rate of stomach cancer in the entire world (4). Both cancers are thought to arise from chronic inflammation caused by Helicobacter pylori (*H. pylori)* (5) or gastroesophageal reflux disease (GERD). This data strongly suggests the great need for alternative therapies against these two types of cancers. MRN-100 is an iron-based compound composed of bivalent and trivalent ferrates. The current study was undertaken to examine the protective effect of MRN-100 against gastric/esophagus cancer in rats.

We have recently examined the protective effect of MRN-100 against the carcinogen methylnitronitrosoguanidine (MNNG)-induced gastric and esophageal cancer in rats for 33 weeks. Results showed that carcinogen MNNG-treated rats caused 85% of rats developed dysplasia and cancer in the gastroesophageal tissues. On the other hand, MRN-100 treatment showed only 40% of rats with dysplasia and cancer (6).



There are several mechanisms by which MRN-100 exerts anti-cancer activity. First, MRN-100 exhibited significant cancer chemopreventive activity by protecting tissues against oxidative damage in rats (6). Increased levels of ROS have been attributed to the initiation of many diseases including cancer and aging. It is of interest to know that MRN-100 exerted an antioxidant effect by increasing levels of glutathione (GSH), antioxidant enzymes superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), and total antioxidant capacity (TAC) level. This was accompanied by a reduction in the total free-radical and malondialdehyde (MDA) levels. The ability of MRN-100 to protect tissues against oxidative stress damage may involve regulating cellular free-iron levels. MRN-100 captures excess iron in the body tissues and stores them in compounds such as ferritin and transferrin, and may prevent excess iron from taking part in the Fenton reaction which results in the prevention of reactive radical accumulation.

The second mechanism that may involve MRN-100 effect against gastric/esophagus cancer is its immune modulatory effect. Cancer patients and healthy subjects who were orally administered MRN-100 showed an enhancement of their natural killer (NK) cell activity (7-9). NK cells are known to play a central role in the first line of defense against cancer and virally infected cells (10,11).

The third mechanism that also contributes to the protective effect of MRN-100 against cancer is its ability to induce an apoptotic effect against gastric cancer cells via a mitochondrial-dependent pathway.

The safety of anti-cancer agents is of major concern. Current anti-cancer drugs are toxic. On the other hand, the biosafety of MRN-100 has been studied in healthy subjects and cancer patients who were administered MRN-100 orally for up to 12 months. The human subjects did not show adverse side effects but rather showed enhancement of immune function (7-9).

In conclusion, MRN-100 exhibited decreased levels of dysplasia and cancer in the gastric/esophagus tissues through mechanisms that involve its ability to act as a potent antioxidant agent. These results may suggest the effectiveness of MRN-100 as an adjuvant for the treatment of gastric/esophageal carcinoma.

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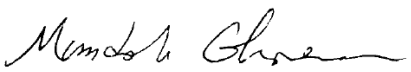

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