13023

Effect of Feeding Wheat Germ Oil on Production of Liver Cancer by Butter-Yellow.

KANEMATSU SUGIURA.

From Memorial Hospital for the Treatment of Cancer and Allied Diseases, New York City.

Yoshida[1] experimentally produced liver cancer in rats by feeding o-aminoazotoluene, and Kinosita,[2] using dimethylaminoazobenzene, commercially known as butter-yellow, produced liver cancer in a much shorter time. In both cases, rice was used as the basal food for the animals. On the other hand, Fischer-Wasels[3] reported that rats receiving o-aminoazotoluene and bread developed only liver cirrhosis.

Recently Kinosita[4] and Okada[5] showed that the production of liver cancer by dimethylaminoazobenzene is definitely reduced when wheat bread was used as basal diet instead of rice. Vassiliadis[6] found that rats receiving o-aminoazotoluene and a diet of wheat flour showed no tumor at the end of a year. Whereas, if the diet consisted solely of rice and dye substance, a large number of adenocarcinoma of the liver appeared. The failure of o-aminoazotoluene to produce liver cancer in rats maintained on the diet of wheat was also shown by Ando.[7] These experiments demonstrate that a certain substance of wheat is antagonizing the carcinogenic action of dimethylaminoazobenzene or of o-aminoazotoluene in the body.

The object of the present study is to find whether or not wheat germ oil has any inhibiting effect upon the production of liver cancer in rats induced by the oral administration of butter-yellow. It was shown in a recent communication[8] that the ether extracts of rice-bran and of brewer's yeast contain a substance which is inhibitory to the development of liver cancer in rats by butter-yellow feeding.

Experimental. In the present series of experiments two samples of wheat germ oil were used. One was prepared in the same manner

1 Yoshida, T., *Proc. Imp. Acad. Japan*, 1932, **8**, 464.
2 Kinosita, R., *Trans. Soc. path. jap.*, 1937, **27**, 665.
3 Fischer-Wasels, B., *Zbt. allg. Path. Anat.*, 1936, **66**, 359.
4 Kinosita, R., *Gann*, 1939, **33**, 225.
5 Okada, D., *Osaka Igaku Zasshi*, 1940, **39**, 485.
6 Vassiliadis, H. C., *Am. J. Cancer*, 1940, **39**, 377.
7 Ando, T., *Gann*, 1940, **34**, 356.
8 Sugiura, K., and Rhoads, C. P., *Cancer Research*, 1941, **1**, 3.

as that of rice-bran oil, *i. e.*, the wheat germ was continuously extracted in Soxhlet extractors with ether for 24 to 48 hours at 50°C. One thousand grams of wheat germ yielded about 70 cc of a yellowish brown oily emulsion. Another sample of wheat germ oil was kindly prepared by Dr. C. Hoffman of Ward Baking Co., N. Y. One hundred cc of the oil represented 900 g of wheat germ. It contained 0.5 gamma of riboflavin (vitamin B_2) per gram of the material.

A group of 10 rats was maintained on the mixture of 95% unpolished rice and 5% of the wheat germ oil prepared here. A second group of 10 rats was maintained on the mixture of 95% unpolished rice and 5% wheat germ oil prepared by the Ward Baking Co. A third group of 20 rats was kept on unpolished rice without wheat germ oil. All animals received butter-yellow (p-dimethylaminoazobenzene) in the proportion of 20 cc of 3% solution in olive oil per 1000 g of food. Each of the 3 groups of rats received a small amount of fresh carrot daily. Each rat consumed approximately 5 to 7 g of food daily.

After 150 days the experiments were discontinued; all rats then living were sacrificed and examined. The results of the experiments are presented in Tables I, II, and III. In all cases the gross diagnoses were confirmed by microscopic examination. Rats used in this study were of the Sherman strain. Rats that died before the period of 60 days are not included in the tables.

TABLE I.
Effect of Feeding Wheat Germ Oil on Production of Liver Cancer by Butter-Yellow.

Rat No.	Sex	No. of days fed	Body weight (g)			Liver findings*
			Initial	Maximum	Final	
1	♀	68	112	112	95	±
2	,,	84	122	122	87	±
3	,,	107	130	130	68	+
4	♂	132	112	132	127	+
5	,,	150	135	143	136	+
6	,,	150	122	122	75	+
7	♀	150	126	126	100	+
8	♂	150	122	143	130	+
9	,,	150	120	129	113	++

* — indicates smooth, practically normal liver; ± indicates nodular cirrhosis with adenomatous hyperplasia; + indicates distinct areas of cholangioma or hepatoma or both; ++ indicate extensive liver cancer with or without metastasis.

The data in Tables I and II show clearly that daily ingestion of wheat germ oil, rich in vitamin E but poor in vitamin B_2 had no protective action upon the production of liver cancer. Of the 16

TABLE II.
Effect of Feeding Wheat Germ Oil (Ward Baking Co.) on Production of Liver Cancer by Butter-Yellow.

Rat No.	Sex	No. of days fed	Body weight (g)			Liver findings*
			Initial	Maximum	Final	
1	♀	70	127	127	80	±
2	,,	101	130	130	70	+
3	♂	106	134	150	86	+
4	,,	114	135	135	70	+
5	♀	114	128	128	77	+
6	♂	141	140	140	109	++
7	♀	150	141	141	128	—
8	,,	150	135	139	125	+
9	♂	150	138	138	120	++
10	,,	150	135	148	136	++

*See Table I for explanation of symbols.

TABLE III.
Effect of Unpolished Rice Alone on Production of Liver Cancer by Butter-Yellow.

Rat No.	Sex	No. of days fed	Body weight (g)			Liver findings*
			Initial	Maximum	Final	
1	♀	66	125	125	75	—
2	,,	66	125	134	110	±
3	♂	68	119	119	88	±
4	♀	68	138	138	97	±
5	♂	74	127	127	70	+
6	♀	85	124	124	107	+
7	♂	103	116	118	70	+
8	♀	105	127	129	100	+
9	,,	107	130	130	68	+
10	,,	109	116	116	69	+
11	♂	124	130	130	70	+
12	♀	143	118	118	60	+
13	♂	150	144	146	145	+
14	,,	150	131	135	100	+
15	♀	150	132	132	83	+
16	♂	150	121	121	105	++
17	♀	150	120	120	109	++

*See Table I for explanation of symbols.

rats which died or were sacrificed between 100 and 150 days after the beginning of the experiment, microscopic examination revealed that 15 animals (94%) had liver cancer, both cholangioma and hepatoma.

The author wishes to express his appreciation to Dr. C. P. Rhoads for his interest and valuable advice.