Effects of 5-Methoxypsoralen (5-MOP) on Arylamine N-Acetyltransferase Activity in the Stomach and Colon of Rats and Human Stomach and Colon Tumor Cell Lines

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Abstract. Background: It has been shown that cytochrome P450 enzymes (CYPs) and acetyltransferase can be used as biomarkers of carcinogen-DNA adduct levels and human cancer susceptibility. The gastrointestinal tract is the portal of entry of foreign compounds and presents xenobiotic metabolizing N-acetyltransferase (NAT) and CYPs activities. 5-Methoxypsoralen (5-MOP) has been used in combination with UV radiation in skin photochemotherapy for decades. A number of studies have demonstrated that 5-MOP is inhibitory towards mouse and human CYP isoforms, but investigations on the direct effects on NAT activity in laboratory animals and human cancer cells are limited. The main objective of this study was to document the effects of 5-MOP on the modulation of NAT activities in the stomach and colon of rats and human stomach and colon tumor cell lines. Materials and Methods: N-Acetylation of 2-aminofluorene (AF) to 2-acetylaminofluorene (AAF) by NAT in the stomach and colon of Sprague-Dawley (SD) rats and in human stomach (SC-M1) and colon (COLO 205) tumor cell lines was investigated. Results: The data show that the metabolic activity of NAT in the rat colon was higher than that in the rat stomach, and the further metabolism of AAF was slower in the stomach than in the colon. 5-MOP increased the activity of NAT and also increased the further metabolism of AAF at 24 h in the rat stomach. In the rat colon, no statistically significant changes caused by 5-MOP were observed in NAT activity, but 5-MOP increased the further metabolism of AAF at 24 to 72 h. 5-MOP decreased the activity of NAT only at 72-h incubation in SC-M1 cells. In COLO 205 cells, however, 5-MOP decreased the activity of NAT between 24 h and 72 h. The optimal concentrations of 5-MOP to induce decreased NAT activity in SC-M1 cells were 0.05 mM to 25 mM. In COLO 205 cells, the data indicate that the higher the concentrations of 5-MOP, the higher the acetylation of AF; a promotion effect of NAT activity occurred at a higher dose (50 mM) of 5-MOP and an inhibition effect occurred at lower doses (0.05-0.5 mM) of 5-MOP, while concentrations of 5-25 mM of 5-MOP showed no significant difference compared with the control regimen. Conclusion: The metabolic activity of NAT in the rat colon was higher than that in the rat stomach, and the results also showed a high degree of correspondence with SC-M1 cells and COLO 205 cells. 5-MOP more efficiently inhibited NAT activity in human stomach and colon tumor cell lines than in the stomach and colon of rats.

A large portion of human cancers are due to exposure to environmental and occupational carcinogens. The arylamine carcinogens represent one of the classes of chemicals known to induce tumors (1-4), and they require metabolic activation by host enzymes. A major metabolic pathway for arylamines is N-acetylation, which is catalyzed by the host cytosolic arylamine N-acetyltransferase (NAT) (1-6).

The major site of arylamine metabolism in the body is the liver, however NAT, an enzyme found mainly in the liver, is involved in several steps of both arylamine activation and detoxification and is also found in many types of human tissues (7, 8). In fact, in mice, the potential N-acetylation capacity of extrahepatic tissue exceeds that of the liver (9). Several carcinogenic arylamines and heterocyclic arylamines are among the known substrates for NAT, and attenuation of NAT activity in the liver has been associated with several disease processes, hence, there is much interest in the role of NAT in chemical carcinogenesis. Two distinct NAT genes (NAT1 and NAT2) in humans have been identified and

Abbreviations: 5-MOP, 5-methoxypsoralen; NAT, N-acetyltransferase; CYPs, cytochrome P450 enzymes; AF, 2-aminofluorene; AAF, 2-acetylaminofluorene; PBS, phosphate-buffered saline; DMSO, dimethyl sulfoxide; EDTA, ethylenediaminetetraacetic acid; DTT, dithiothreitol; PMSF, phenylmethylsulfonylfluoride; HPLC, high-performance liquid chromatography; SD rats, Sprague-Dawley rats.

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Key Words: 5-Methoxypsoralen, 2-aminofluorene, 2-acetylamino-fluorene, N-acetyltransferase.
Recently, our laboratory found that 5-MOP affects the activity of NAT. Because diet may influence the levels of NAT activity in laboratory animals and human cancer cells (49, 51, 53-58), investigations into the direct effects of 5-MOP on NAT activity in colon tissues including the stomach and colon (8), the current interest is to study the effect of 5-MOP on arylamine N-acetyltransferase activity in the stomach and colon of rats and in human colon and stomach tumor cell lines. In particular, it is of interest to study the effect of 5-MOP on arylamine N-acetyltransferase activity in the stomach and colon of rats and in human colon and stomach tumor cell lines.

Materials and Methods

Chemicals and reagents. 5-Methoxypsoralen (5-MOP), 2-amino-fluorene (AF), 2-acetylaminofluorene (AAF), leupeptin, dithiothreitol (DTT), ethylenediaminetetraacetic acid (EDTA), phenylmethylsulfonylfluoride (PMSF), RPMI 1640 medium and Tris-HCl were purchased from Sigma Chemical Co. (St. Louis, MO, USA). Acetonitrile, dimethyl sulfoxide (DMSO) and potassium phosphates were obtained from Merck Co. (Darmstadt, Germany). Penicillin/streptomycin, fetal calf serum and trypsin-
The retention time was 9.5 min for AF and 6.8 min for AAF. All studies were carried out at 25°C on a 12-h light/dark cycle. The cages were kept under controlled airflow conditions to prevent contamination of the specimens. The sample amounts of AF and AAF were injected onto a C18 reversed-phase column (Spherisorb 4.6 x 250 nm) of a performance liquid chromatography (HPLC) system. The elution peak was compared with that of known standards. The human colon adenocarcinoma cell line (COLO 205, from a 70-year-old male Caucasian) was obtained from the Chinese Culture Collection (Hsinchu, Taiwan). The cells were placed into 75-cm² tissue culture flasks and grown in RPMI 1640 medium, supplemented with 10% fetal bovine serum, containing penicillin and streptomycin (100 μg/mL) and 1 mM glutamine, at 37°C in a humidified atmosphere of 5% CO2 and 95% O2.

### Table 1. Comparisons of the concentrations of the relative samples' AF and AAF in cytosol of stomach and colon of rats after oral AF and with or without 5-MOP co-treatment for various times.

<table>
<thead>
<tr>
<th>Stomach</th>
<th>AF (nmol/g tissue)</th>
<th>Colon</th>
<th>AAF (nmol/g tissue)</th>
<th>AF (nmol/g tissue)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12A</td>
<td>3.5124±1.1479</td>
<td>12A</td>
<td>1.2074±0.1550***</td>
<td>0.4099±0.1256</td>
</tr>
<tr>
<td>12B</td>
<td>2.6484±0.1073</td>
<td>12B</td>
<td>0.2344±0.0494</td>
<td>0.2001±0.1655</td>
</tr>
<tr>
<td>12C</td>
<td>2.7346±0.2103</td>
<td>12C</td>
<td>0.7782±0.1921**</td>
<td>0.1685±0.0411</td>
</tr>
<tr>
<td>24A</td>
<td>0.1849±0.1044</td>
<td>24A</td>
<td>1.5315±0.5803</td>
<td>ND</td>
</tr>
<tr>
<td>24B</td>
<td>0.1600±0.0998</td>
<td>24B</td>
<td>0.9283±0.3635</td>
<td>ND</td>
</tr>
<tr>
<td>24C</td>
<td>0.0575±0.0283***</td>
<td>24C</td>
<td>0.0751±0.0271**</td>
<td>ND</td>
</tr>
<tr>
<td>48A</td>
<td>0.1005±0.2251</td>
<td>48A</td>
<td>0.0461±0.0101</td>
<td>ND</td>
</tr>
<tr>
<td>48B</td>
<td>0.0875±0.0198</td>
<td>48B</td>
<td>0.0407±0.0121</td>
<td>ND</td>
</tr>
<tr>
<td>48C</td>
<td>0.0759±0.0041</td>
<td>48C</td>
<td>0.007±0.0013**</td>
<td>ND</td>
</tr>
<tr>
<td>72A</td>
<td>0.1847±0.0378**</td>
<td>72A</td>
<td>0.0366±0.0121</td>
<td>ND</td>
</tr>
<tr>
<td>72B</td>
<td>0.0588±0.0159</td>
<td>72B</td>
<td>0.0430±0.0100</td>
<td>ND</td>
</tr>
<tr>
<td>72C</td>
<td>0.1222±0.0134**</td>
<td>72C</td>
<td>ND**</td>
<td>ND</td>
</tr>
</tbody>
</table>

Rats were treated with 0.5 mmol/Kg 5-MOP and 0.3 mmol/Kg AF for 12, 24, 48 and 72 h. The rats were sacrificed for different tissues and AF and AAF were determined as described in "Materials and Methods". A=contrast regimen, received AF only. B=control regimen, received DMSO (solvent) and AF. C=5-MOP regimen, received 5-MOP (dissolved in DMSO) and AF. Data are expressed as mean±SD, n=6, and values significantly different from the control value: *p<0.05, **p<0.01, ***p<0.001, ND=not detectable.

### In vivo

A total of 72 rats were subjected to 3 different regimens, each regimen divided into 4 groups with 6 rats in each group. Gastric intubation was used for delivery of the test compounds into each animal. The first regimen received 1 mL 5-MOP (dissolved in DMSO) at a dose of 0.5 mmol per Kg of body weight. Regimen 2, the control regimen, received only 1 mL solvent (DMSO), without any 5-MOP. Regimen 3, the contrast regimen, received nothing at that time. Twenty-four hours later, all of the rats from the 3 regimens received 1 mL AF (dissolved in DMSO) at a dose of 0.3 mmol per Kg of body weight. The groups were divided by different collecting time: 12, 24, 48 and 72 h after AF administration, and then the animals were transferred to individual metabolism cages. The stomachs and the colons of the rats from each regimen were collected and were immediately extracted with ethyl acetate/methanol (95:5). The solvent was evaporated and the residue redissolved in methanol and assayed for AF and AAF by HPLC, as described above.

### Human colon tumor cell line

The human colon adenocarcinoma cell line (COLO 205, from a 70-year-old male Caucasian) was obtained from the Taipei Veterinary Hospital (Taipei, Taiwan). The cells were placed into 75-cm² tissue culture flasks and grown in RPMI1640 medium, supplemented with 10% fetal bovine serum, containing penicillin and streptomycin (100 μg/mL) and 1 mM glutamine, at 37°C in a humidified atmosphere of 5% CO2 and 95% O2.

### Human stomach tumor cell line

The human stomach adenocarcinoma cell line (SC-M1) was obtained from the Hsinchu Culture Collection Center (Hsinchu, Taiwan). The cells were placed into 75-cm² tissue culture flasks and grown in RPMI 1640 medium, supplemented with 10% fetal bovine serum, containing penicillin and streptomycin (100 μg/mL) and 1 mM glutamine, at 37°C in a humidified atmosphere of 5% CO2 and 95% O2.
Drug treatment. SC-M1 and COLO 205 cells were treated with different concentrations of 5-MOP (0.05, 0.5, 5, 10, 25 and 50 mM) and incubated for 72 h for the dose-effect study of 5-MOP on NAT activity. To determine the time-course effect of 0.5 mM 5-MOP on NAT activity, the cells were incubated at 37 °C and harvested at 12, 24, 48 and 72 h, respectively. 5-MOP was dissolved in DMSO and the final concentration of vehicle was <0.1%. Only DMSO (solvent) was added for the control regimen.

Intact cell NAT activity determination. The human stomach and colon tumor cells in RPMI 1640 medium were incubated with 2 mM AF at a concentration of 1% at 1x10⁶ cells/mL in individual wells of 6-well cell culture plates, with or without 5-MOP co-treatment, at 37 °C in a humidified atmosphere of 5% CO₂ and 95% O₂. At the end of the incubation, the cells and medium were removed and centrifuged. For experiments with AF and AAF, the supernatant was immediately extracted with ethylacetate/methanol (95:5), the solvent was evaporated and the residue was redissolved in 50 µL methanol and was assayed for AF and AAF by HPLC, as described above. All reactions of experiments and controls were run in triplicate.

Statistical treatment of data. The analysis of the data was performed with an unpaired Student’s t-test and linear regression.

Results

Effects of 5-MOP on arylamine N-acetyltransferase activity in the stomach and colon cytosol of rats. The comparisons of the concentrations of the relative samples’ AF and AAF, with or without 5-MOP co-treatment, are presented in Table I. Gastric intubation of AF was employed in this experiment, therefore large amounts of AF of the stomach were detected. The level of AF was high in the stomach at 12 h, but it had decreased rapidly at 24 h, and stayed at a low concentration during the 24- to 72-h period in all 3 regimens. AF was not detected in the colons at the 24- to 72-h time-periods in all 3 regimens. The results indicated that the stomach and colon metabolize AF rapidly. The metabolic activity of NAT of the rat colon was higher than that of the stomach, and 5-MOP caused a decrease of AF concentration in the stomach at the 24-h time-period. The concentrations of AAF in the stomach and colon were low. Although DMSO (solvent) influenced the metabolism of AAF, compared with the control regimen, 5-MOP still caused an increase in the further metabolism of AAF, and a decrease in the concentration of AAF in the stomach at 24 h, and in the colon during the 24- to 72-h time-period.

Effects of various concentrations of 5-MOP on NAT activity both in SC-M1 and COLO 205 cells for 72-h incubation. The possible effects of 5-MOP on NAT activity both in SC-M1 and COLO 205 cells for 72-h incubation were examined by HPLC. The means±SD of the concentration of AAF, co-treated with or without various concentrations of 5-MOP (0.05-50 mM), were compared with the control regimen, and values significantly different from the control value: *p<0.05, **p<0.01, ***p<0.001.
The percentage of acetylation of AF on intact SC-M1 and COLO 205 cells at various concentrations of 5-MOP. The possible effects of 5-MOP on NAT activity, both in SC-M1 and COLO 205 cells, were examined by HPLC, assessing the percentage of acetylation of AF. SC-M1 cells, with or without specific concentrations of 5-MOP (0.05-50 mM) co-treatment, showed different percentages of AF acetylation (Figure 1). While there was no obvious relationship between the dose of 5-MOP and the percentage of acetylation ($r=0.6333$), according to the data, concentrations of 5-MOP from 0.05 mM to 25 mM showed an inhibition effect on the acetylation. COLO 205, with or without specific concentrations of 5-MOP (0.05-50 mM) co-treatment, showed different percentages of AF acetylation (Figure 2). The data indicates that 5-MOP induced a dose-dependent effect in our experimental concentrations on COLO 205 cells ($r=0.8912$); a promotion effect at a higher dose (50 mM) and an inhibition effect at lower doses (0.05-0.5 mM), while the concentrations 5-25 mM had no significant difference compared with the control regimen. In other words, the higher the concentration of 5-MOP, the higher the acetylation of AF.

**Table III. Effects of incubation time on AAF production by SC-M1 and COLO 205 cells.**

<table>
<thead>
<tr>
<th></th>
<th>SC-M1</th>
<th>COLO 205</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 h</td>
<td>0.482±0.004</td>
<td>12.732±0.142</td>
</tr>
<tr>
<td>24 h</td>
<td>0.483±0.14</td>
<td>8.908±0.692</td>
</tr>
<tr>
<td>48 h</td>
<td>0.65±0.004</td>
<td>10.444±1.000</td>
</tr>
<tr>
<td>72 h</td>
<td>0.720±0.025</td>
<td>10.686±0.666</td>
</tr>
</tbody>
</table>

**Effects of 5-MOP on NAT activity both in SC-M1 and COLO 205 cells for 12, 24, 48 and 72-h incubation.** Data are expressed as mean±SD, n=3, and values significantly different from the control value: *$p<0.05$, **$p<0.01$.**

The optimal concentrations of 5-MOP for both SC-M1 and COLO 205 cells on NAT inhibition were 0.05 and 0.5 mM, so 0.5 mM of 5-MOP was chosen to determine the time-course effect on NAT activity in SC-M1 and COLO 205 cells. The cells were incubated at 37°C and harvested at 12, 24, 48 and 72 h, respectively. The NAT activity was determined by the AAF produced. In SC-M1 cells, an increased time of incubation led to increased AAF production up to 72 h ($r=0.9735$), while

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![Figure 2](image2.png)

**Figure 2. Effects of 5-MOP on AF acetylation of COLO 205 cells.** The COLO 205 cells were incubated as described for 72 h at the concentration of AF and co-treatment with or without various concentrations of 5-MOP (0.05-50 mM). AF and AAF were measured by HPLC assays and calculated for percentages of AF acetylation. Data are expressed as mean±SD, n=3, and values significantly different from the control value: *$p<0.05$, **$p<0.01$.**

![Figure 3](image3.png)

**Figure 3. Time-course effects on AF acetylation in SC-M1 cells.** The tumor cells were incubated for 12, 24, 48 and 72 h with or without 0.5 mM 5-MOP co-treatment. AF and AAF were measured by HPLC assays and calculated for percentages of AF acetylation; the NAT activity was determined by the percentage of acetylation of AF. Each point represents the mean of triplicate assays of 3 incubations of cells. Data are expressed as mean±SD and values significantly different from the control value: **$p<0.01$.**
5-MOP caused a decrease of the AAF production only at the 72-h time-period. In COLO 205 cells, no time-course effect was found \( r=-0.2434 \), but the 5-MOP decreased the AAF production during the 24- to 72-h time-period (Table III).

The percentage of acetylation of AF on intact SC-M1 and COLO 205 cells at various incubation time-periods showed different percentages of AF acetylation (Figures 3 and 4). The cells were incubated at 37°C and harvested at 12, 24, 48 and 72 h, respectively. The NAT activity was determined by the percentage of acetylation of AF. In SC-M1 cells, an increased time of incubation led to increased AF acetylation up to 72 h \( r=0.9715 \), and 5-MOP decreased acetylation only at the 72-h time-period. In COLO 205 cells, no time-course effect was found \( r=-0.1020 \). 5-MOP decreased the AF acetylation during the 24- to 72-h time-period, but from the 24-h to 72-h time-periods, 5-MOP showed a time-course effect \( r=0.9100 \).

**Discussion**

The majority of food-derived and environmental chemicals that have been postulated to be causative agents in the development of certain forms of human cancer require metabolism to exert their mutagenic and carcinogenic effects. The ability of a particular arylamine to be transformed to a carcinogenic end-product is likely to be strongly dependent upon the relative tissue levels of NAT1, NAT2 and CYPs capable of detoxifying or activating this class of chemical agent (49).

The gastrointestinal tracts are the portals of entry for foreign compound; they observe xenobiotic metabolizing of NAT and CYPs. These enzymes not only contribute to first-pass clearance, but may also influence the tissue burden of foreign compounds. In previous studies, it was demonstrated that, in the human stomach, the surface columnar epithelial cells exhibited a NAT1 signal, and in the colon, expression of NAT1 and NAT2 was observed in the columnar epithelial cells and in epithelial cells of the crypts of Lieberkühn (7, 8). In rats, NAT mRNA has been shown to be predominantly localized to the basal areas of gastric glands in the stomach and the differentiated surface epithelial cells of the colon (59). The most prominent CYPs occurring in the human stomach and colon are CYP1A and CYP3A (60). The coincident expression of these enzymes in the stomach and colon plays a role in the bioactivation of gastric and colon carcinogens, and the susceptibility markers of cancer development, carcinogen-metabolizing enzymes such as NAT and CYPs, have been analyzed in gastric cancer and colon cancer patients (61, 62).

5-MOP, in combination with newly-developed UV irradiation systems that emit high-intensity UVA radiation in the treatment of severe psoriasis, mycosis fungoides and over 16 other skin diseases, emerged as a photochemoprotective agent against non-melanoma skin cancers and as an immunological modifier in the management of certain patients with disorders of circulating T-cells using new techniques of photopheresis (37). Several recent reports have investigated the role of 5-MOP in relation to CYPs. 5-MOP significantly reduced the total CYP-specific content in the liver (42). It is also an inhibitor and inactivator of CYP2A6 (51) and CYP2BI (52), while lack of enzymatic activity of CYP2A6 is associated with gastric adenocarcinoma among the Japanese population (53). CYP2A6 has been shown to be an important pathway responsible for the metabolism of certain nitrosamines in the liver; lacking this activity would inhibit first-pass clearance of ingested nitrosamines, resulting in greater levels of these carcinogens in the stomach (54). 5-MOP contains a furan ring, which has been suggested to be the group responsible for the inactivation of CYP1A2 (55), while CYP1A2 may play a role in the early stages of gastric carcinogenesis by activating nitrosamines to mutagenic products (56). Furthermore, colon cancer risk is associated with CYP1A2 (49), 5-MOP may contribute to the inhibitory effect on CYP3A4 (57, 58), and 5-MOP was also shown to produce mechanism-based inhibition of CYP3A4 (58). CYP3A is the largest subfamily of the CYP enzymes expressed in the human liver and gastrointestinal tract.
CYP3A4 has been found in human colon and the colon carcinoma cell line LS180, as well as in stomach cancer (60). CYP3A4 may constitute the focal point for regulation by several nuclear receptors that mediate cellular detoxification and, thus, afford chemoprotection against xeno- and endobiotics in a number of different tissues (64). CYP3A4 also plays a role in gastric carcinogenesis by activating nitrosamines to mutagenic products (56), and recent studies have shown that prehepatic activation of carcinogens by CYP3A could lead to the transformation of intestinalized mucosa to cancer of the stomach (65). There are well-documented reports on the inhibition of stomach- and colon-associated CYPs of 5-MOP, but the direct effects on NAT activity in laboratory animals and human cancer cell lines are unclear. In the present study, we demonstrated the possible effects of 5-MOP on the N-acetylation of AF of the lines are unclear. In the present study, we demonstrated the possible effects of 5-MOP on the N-acetylation of AF of the stomach and colon in vivo and in vitro, based on the concentrations of the amount of substrates (AF) and acetylated products (AAF). In the control regimen, the total concentration of the AF in the stomach was higher than in the colon at 4 time-periods, respectively, according to the consumption rate of AF. This indicates that the metabolic activity of NAT was lower in the stomach than in the colon. The total concentration of AAF in the stomach was higher than in the colon at various time-periods (12 h, 48 h and 72 h), indicating that the further metabolism of AAF was slower in the stomach than in the colon. In the stomach, our results demonstrated that 5-MOP increased the activity of NAT and also increased the further metabolism of AAF at 24 h in the stomach. 5-MOP showed the inhibitory effect in further metabolism of AAF at the 72-h time-period. In the colon, no statistically significant changes affected by 5-MOP were observed in NAT activity, and 5-MOP increased the further metabolism of AAF at 24 to 72 h, but the inhibitory effect was shown at 12 h. The inhibitory effect of 5-MOP on further metabolism of AAF occurred at late time-periods in the stomach, but in the colon the effect occurred at earlier periods in vivo. 5-MOP was more efficient at increasing the further metabolism of AAF for the experimental time-periods in rat colons than in rat stomachs.

Arylamine NAT activity towards AF was detected in human colon tumor cell lines (21, 28); however, in the human stomach tumor cell line there are no reports that any factors would affect tumor cell NAT activity. According to the N-acetylation rate of AF in in vitro studies, NAT was activated more in COLO 205 cells than in SC-M1 cells. These results show a high degree of correspondence with in vitro studies. The optimal concentrations of 5-MOP for inducing decreased NAT activity in SC-M1 cells were 0.05 mM to 25 mM. In COLO 205 cells, they were 0.05 mM and 0.5 mM, while at 50 mM, 5-MOP showed a promotion effect of NAT activity. 5-MOP is more efficient when administered on a time-course in COLO 205 cells than in SC-M1 cells.

In conclusion, NAT and CYP expression are generally regarded as relevant biomarkers of carcinogen exposure and their levels in target tissues have often been predictive of tumor incidence in experimental animals and various tumor cell lines (16, 17, 53, 55, 56). Thus, human risk assessment procedures have utilized dose-response models that assume proportional relationships between carcinogen exposure and cancer susceptibility, even though wide inter-individual variations in human metabolic activating enzymes have now been clearly established. To evaluate these approaches, we examined the NAT activity of the stomach and colon in vivo and human stomach and colon tumor cell lines in vitro and the role that 5-MOP plays in this process. The results demonstrated that 5-MOP was more efficient in affecting NAT activity in human stomach and colon tumor cell lines than in the stomach and colon of rats. It is not known whether allowing 5-MOP to reduce NAT activity will decrease tumor production or whether 5-MOP might prevent the development of stomach and colon cancer. Other investigators have demonstrated that elevated levels of NAT activity are associated with sensitivity to the mutagenic effects of many arylamines (66). 5-MOP reduces the rate of substrate acetylation by NAT, and may or may not reduce the risk of tumor formation. It may depend on whether or not the host is exposed to the arylamine carcinogens. In this case the decreased NAT activity may lead to a reduction in the risk of tumor formation. The present results offer some evidence that 5-MOP decreases the NAT activity in intact human stomach and colon tumor cells. Although 5-MOP has shown an inhibition effect on CYPs, the in vivo study revealing that further metabolism of AAF was promoted in the colon of the rats may mean that other parameters are also involved in AAF metabolism. In conclusion, investigation of the impact of 5-MOP on NAT activity has shown that 5-MOP may play a role in chemoprotection against xenobiotics in the stomach and the colon.

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References


