INHIBITION OF THE MUTAGENIC EFFECTS OF SULFATIAZOLE-NITRITE MIXTURE BY L-ASCORBIC ACID AND GREEN TEA

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INTRODUCTION

The concept of chemoprevention (use of natural or synthetic compounds to prevent cancers) has great appeal. N-nitroso compounds are mutagens which can be formed in vivo due to the reaction between amides and/or amines with nitrite (1). L-ascorbic acid (asc.) and green tea polyphenols can react with nitrite diminishing or removing the nitrosation risk. Sulfonamides, widely used by their properties, present potential risk of nitrosation in stomach because the presence of these functions. In the present work we assay the chemopreventive action of asc. and green tea as antimutagens (AM) on the mutagenicity of a reaction mixture (RM) formed by sodium sulfathiazole (NaST) and NaNO\textsubscript{2} in acidic medium, whose mutagenicity was previously proved by us (2).

MATERIALS AND METHODS

Mutagenicity activity was evaluated in a bacterial reverse mutation assay by the standard Ames test (3). Variable doses of asc. 0.0244 M were tested. Aqueous extracts of green tea were prepared with commercial bags of 2 g in 100 mL of sterile distilled hot water, and were diluted 1/5 previous to test.

RESULTS

Results of reversion coefficient, R.C. (R.C. = revertants with tested substance/spontaneous revertants) and % inhibition of mutagenicity of the RM by asc. are shown in Table 1. The % of inhibition (%inh.) was calculated with the following equation: \(\text{% inh.} = \left[\frac{(\text{CR}_{\text{without AM}} - \text{CR}_{\text{with AM}})}{(\text{CR}_{\text{without AM}} - 1)}\right] \times 100\). According to the Ames test a compound would be a mutagen if the R.C. is \(\geq 2\). The R.C. diminished with the tested doses of asc., increasing the % of inhibition of the mutagenicity. In previous work (580-5800 and 5.8-58 nmol L-ascorbic acid/plate) we obtained an inhibition of 34% of mutagenicity in the minor range and 100% in the major one. In the present work good curves dose-response were obtained for the inhibition of mutagenicity of RM in the tested range.

With green tea the R.C. increased with the minor doses and diminished only for the major ones, in agreement with that only a strong green tea might inhibit the formation of nitrosamines (4).

CONCLUSIONS

Total inhibition of the mutagenicity of the reaction mixture NaST-NaNO\textsubscript{2} was achieved for equimolar quantity of L-ascorbic acid with nitrite. Only partial inhibition was achieved with diluted aqueous extract of green tea.

ACKNOWLEDGMENTS

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REFERENCES

Table 1. Effect of the L-ascorbic acid on the mutagenicity of sodium sulfathiazole-NaNO₂ reaction mixture with *Salmonella typhimurium* TA98 strain

<table>
<thead>
<tr>
<th>L-ascorbic acid /plate nmol (µg)</th>
<th>R.C.* exp 1</th>
<th>% inh* exp 1</th>
<th>R.C.* exp 2</th>
<th>% inh* exp 2</th>
<th>R.C.* exp 3</th>
<th>% inh* exp 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>3.17</td>
<td>0</td>
<td>3.27</td>
<td>0</td>
<td>4.41</td>
<td>0</td>
</tr>
<tr>
<td>119 (21)</td>
<td></td>
<td></td>
<td>2.56</td>
<td>31</td>
<td></td>
<td></td>
</tr>
<tr>
<td>363 (64)</td>
<td>2.62</td>
<td>25</td>
<td>1.63</td>
<td>72</td>
<td>2.05</td>
<td>69</td>
</tr>
<tr>
<td>727 (128)</td>
<td>1.70</td>
<td>68</td>
<td>1.20</td>
<td>91</td>
<td>1.93</td>
<td>73</td>
</tr>
<tr>
<td>1215 (214)</td>
<td>1.35</td>
<td>84</td>
<td>1.17</td>
<td>92</td>
<td>1.23</td>
<td>93</td>
</tr>
<tr>
<td>1703 (300)</td>
<td>0.89</td>
<td>100</td>
<td>0.89</td>
<td>92</td>
<td>1.23</td>
<td>93</td>
</tr>
</tbody>
</table>

*R.C.: reversion coefficient = revertants with tested substance/spontaneous revertants; % inhibition of mutagenicity, calculated as follow: % inh. = \([(CR_{without AM} - CR_{with AM})/ (CR_{without AM} - 1)] \times 100 \)

*Only reaction mixture: sodium sulfathiazole/plate: 539 nmol (164 µg); NaNO₂/plate: 1740 nmol (120 µg).

Negative control: without tested compounds, spontaneous revertants/plate ± SD: exp1: 32.5 ± 2.5; exp2: 21.7 ± 2.4; exp3: 27.00 ± 5.6. Positive controls with 4-Nitro-o-phenylenediamine (diagnostic mutagen): R.C.: 3.19