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<td><strong>Author(s)</strong></td>
<td>Wu, J; Lu, H; Zhou, Y; Qiao, L; Ji, R; Wang, AQ; Liu, WM; Xue, QJ</td>
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Effect of 2-(3-carboxy-1-oxopropyl) amino-2-deoxy-D-glucose on human esophageal cancer cell line

Jing Wu, Hong Lu, Yun Zhou, Liang Qiao, Rui Ji, Ai-Qing Wang, Wei-Min Liu, Qun-Ji Xue

INTRODUCTION

2-(3-carboxy-1-oxopropyl) amino-2-deoxy-D-glucose (COPADG, structure is shown in Figure 1) is a derivative of D-glucose, a monose derivative of degraded chitosan. Previous researches have discovered that some amino-D-glucose derivatives are capable of inducing leukemia K562 cells to differentiate into macrophages [1], but their efficacy in inducing apoptosis of tumor cells remains unclear. We conducted this study to determine whether COPADG could inhibit the proliferation of human esophageal cancer cell line Eca-109, to provide experimental evidence for new drug development for esophageal cancer therapy.

MATERIALS AND METHODS

Materials

COPADG, synthesized by the Lanzhou Institute of Chemical Physics of Chinese Academy of Sciences, was dissolved in distilled water, filter-sterilized with 0.22 µm filter disc, and stored at 4 °C until use. Eca-109 cells were purchased from Shanghai Institute of Cell Biology of Chinese Academy of Sciences. RPMI 1640 medium, agarose, trypsin and fetal bovine serum (FBS) were obtained from Gibco BRL Company, and the reagents for MTT assay were purchased from Sigma Chemical Co. Ltd.

Cell culture

Eca-109 cells growing in logarithmic phase were cultured in RPMI 1640 medium supplemented with 100 µL/L heat-inactivated FBS, 100 µg/mL penicillin and 100 µg/mL streptomycin. The cell cultures were maintained in a humidified atmosphere containing 5% CO2 at 37 °C. The medium was replaced every 48 h.

MTT colorimetric assay

MTT assay [2] is based on the enzymatic reduction of the tetrazolium salt MTT in viable and metabolically active cells. Cells at 85% to 100% confluency were harvested with a mixture of 2.5 g/L trypsin and 0.2 g/L EDTA solution and seeded into a 96-well plate at a density of 4×10^3 /well, followed by incubation of the cells with COPADG at varied concentrations (0.01-0.09 mol/L) for different lengths of time (24-96 h, Table 1).

RESULTS

RESULTS: Effects of COPADG on Eca-109 cells cultured in RPMI 1640 medium were examined by a tetrazolium-based colorimetric assay (MTT assay).

RESULTS: COPADG inhibited the growth of Eca-109 cells in a dose- and time-dependent manner; the maximum inhibition rate was 83.75%.

CONCLUSION: COPADG can directly inhibit the proliferation of Eca-109 cells, which may serve as the experimental evidence for development of new drugs for esophageal cancer therapy.

Abstract

AIM: To determine whether 2-(3-carboxy-1-oxopropyl) amino-2-deoxy-D-glucose (COPADG), a derivative of D-amino-glucose, inhibited the growth of human esophageal cancer cell line Eca-109.

METHODS: Effects of COPADG on Eca-109 cells cultured in RPMI 1640 medium were examined by a tetrazolium-based colorimetric assay (MTT assay).

RESULTS: COPADG inhibited the growth of Eca-109 cells in a dose- and time-dependent manner; the maximum inhibition rate was 83.75%.

CONCLUSION: COPADG can directly inhibit the proliferation of Eca-109 cells, which may serve as the experimental evidence for development of new drugs for esophageal cancer therapy.


http://www.wjgnet.com/1007-9327/10/3380.asp

Figure 1 Chemical structure of 2-(3-carboxy-1-oxopropyl) amino-2-deoxy-D-glucose.
Table 1 Inhibitory effect of COPADG on the proliferation of esophageal cancer cell line Eca-109 (mean±SD)

<table>
<thead>
<tr>
<th>Concentration (mol/L)</th>
<th>24 h</th>
<th>48 h</th>
<th>72 h</th>
<th>Inhibitory rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 (Control)</td>
<td>1.505±0.090</td>
<td>1.686±0.067</td>
<td>1.745±0.077</td>
<td>12.76</td>
</tr>
<tr>
<td>0.01</td>
<td>1.313±0.053 b,c</td>
<td>1.336±0.057 b</td>
<td>1.199±0.083 c</td>
<td>36.35</td>
</tr>
<tr>
<td>0.03</td>
<td>0.958±0.028</td>
<td>0.966±0.068</td>
<td>0.900±0.056</td>
<td>73.42</td>
</tr>
<tr>
<td>0.05</td>
<td>0.400±0.064 b,c</td>
<td>0.429±0.065 a</td>
<td>0.384±0.050 b,c</td>
<td>74.55</td>
</tr>
<tr>
<td>0.07</td>
<td>0.383±0.045</td>
<td>0.360±0.039</td>
<td>0.342±0.037</td>
<td>76.41</td>
</tr>
<tr>
<td>0.09</td>
<td>0.355±0.046 b,c</td>
<td>0.362±0.053 c</td>
<td>0.280±0.039 c</td>
<td>12.76</td>
</tr>
</tbody>
</table>

At the same time point, P<0.01 vs the control group; bP<0.01 vs 0.03 mol/L; cP<0.05, P>0.05 vs 0.07 mol/L.

an obvious time-and dose-dependent manner when the COPADG concentrations were below 0.05 mol/L, and higher concentrations tended to induce gradually stabilized inhibition, suggesting a saturation of the effects of COPADG (Table 1, Figure 2).

Figure 2 Inhibition of Eca-109 cell growth by COPADG.

DISCUSSION

COPADG is a derivative of D-glucose, which is a low-molecular-weight compound with multiple biological activities and a monosaccharide derived from chitosan through release of an acetyl group followed by degradation of the residual group. D-glucose is the intermediate during the synthesis of protein-polysaccharide macromolecules, and distributed in almost every human tissue as a part of the structural components of cell membrane and tissues. From the biological standpoint, D-glucose not only is involved in hepatic and renal detoxification against toxic agents, but also acts to stimulate the anti-inflammatory response and enhance the synthesis of protein-polysaccharides. Studies\(^3,4\) have also shown that D-glucose could inhibit tumor cell growth, and partial derivatives of D-glucose could potently induce differentiation of tumor cells. Some D-amine-glucose derivatives were able to induce leukemia K562 cells to differentiate into macrophages\(^5\), but this effect failed to be observed in human hepatocellular carcinoma cell line\(^6\). Currently, COPADG has become a new focus of interest in cancer therapy.

By conducting this study, we aimed to test whether COPADG, the newest derivative of D-glucose, had any effect on the proliferation of human esophageal cancer cells. MTT assay showed that COPADG could effectively inhibit Eca-109 cell proliferation, in a marked time- and dose-dependent manner below the concentration of 0.05 mol/L: the maximum inhibition rate was 83.75%. The inhibition, however, became stable when the concentrations were higher than 0.05 mol/L, indicating that the effects of the drug might be saturated at this concentration.

The development of cancer has been considered to be the combined results of unrestricted cell proliferation and impairment of normal cell apoptosis\(^6\). These concepts provide a basis for the development of new strategies for cancer treatment. Agents with antiproliferative properties and proapoptotic effects have been widely investigated as potential chemotherapeutic options\(^7,8\).

Conclusion, COPADG has obvious time- and concentration-dependent inhibitory effects against the proliferation of human esophageal cancer cell line Eca-109 \textit{in vitro}, but whether this effect can be achieved in other cell lines still awaits further examination, which may also be necessary to clarify the mechanism underlying this effect.

REFERENCES