



## Cytotoxicity and cellular uptake of perfluorocarboxylic acids



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### ABSTRACT

To address the health and environmental concerns associated with perfluorocarboxylic acids, the assessment of cytotoxicity and bioaccumulation of perfluorocarboxylic acids is essential. This study investigated the effect of perfluorocarboxylic acids having various chain lengths on mouse melanoma B16 cells. The extent of cytotoxicity of perfluorohexanoic acid (C6), perfluoroheptanoic acid (C7), perfluorooctanoic acid (C8), perfluorononanoic acid (C9) and perfluorodecanoic acid (C10) within a concentration range of 0.25–1600  $\mu\text{g/ml}$  was determined. Based on results, the viability of cells was 90% or higher in the presence of C6, C7, C8 at a concentration of up to 200  $\mu\text{g/ml}$ , indicating that B16 cells are safe in the presence of C6, C7 and C8. On the other hand, moderate cytotoxicity was observed with C9 or C10, even at a relatively low concentration of 25  $\mu\text{g/ml}$ . When cells were incubated in the presence of the same concentration (100 or 200  $\mu\text{g/ml}$ ) of perfluorocarboxylic acids, the number of live cells decreased as the perfluoroalkyl chain length increased suggesting that long-chained perfluorocarboxylic acids are more cytotoxic than short-chained perfluorocarboxylic acids. The correlation between cellular uptake and perfluoroalkyl chain length was also investigated. The presence of C6 in the cells was not detected probably because of poor uptake. On the other hand, the presence of C7–C10 in the cells was confirmed and quantified by LC ESI MS. Results showed that cellular uptake of long-chained perfluorocarboxylic acids were significantly higher than short-chained perfluorocarboxylic acids.

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### 1. Introduction

Perfluorocarboxylic acids are widely used in a variety of industrial and consumer products due to their chemical and thermal stability [1]. They are ideal surfactants that can lower the surface tension of water. They are exceptionally stable due to the presence of multiple carbon-fluorine bonds. However, the environmental and health concerns associated with synthetically available perfluorocarboxylic acids such as perfluorooctanoic acid restrict their use. They are classified as persistent organic pollutants (POP) and have been detected in lakes and ocean [2]. They resist degradation by natural processes such as metabolism, hydrolysis, photolysis, or biodegradation that make them remain indefinitely in the environment. Moreover, the reported half-life of perfluorocarboxylic acids takes several years. For instance, the half-life of perfluorooctanoic acid is 3 years.

Another risk associated with perfluorocarboxylic acids is bioaccumulation in human and in animal tissues. In humans, perfluorinated carboxylic acids concentrate in the blood, liver and

kidney [3]. They cause adverse effects on liver and pancreas. Several reports confirmed the carcinogenic, immunotoxic and hepatotoxic effects of perfluorocarboxylic acids [4]. Their use has been restricted during the last decade and several researches were conducted to monitor exposure and tolerance levels of living organisms to the perfluoroalkyl carboxylic acids.

This study was carried out to investigate the effect of several perfluorocarboxylic acids on animal cells. Mouse B16 melanoma cells were incubated in the presence of perfluorohexanoic acid (C6), perfluoroheptanoic acid (C7), perfluorooctanoic acid (C8), perfluorononanoic acid (C9), and perfluorodecanoic acid (C10), and cytotoxicity at various concentrations was investigated. Moreover, cellular uptake of perfluorocarboxylic acid was assessed and the amount present in cells was quantified by LC ESI MS [5].

### 2. Results and discussion

#### 2.1. Cytotoxicity of perfluorocarboxylic acids

The cytotoxicity of perfluorocarboxylic acids was investigated from a concentration range of 0.25–1600  $\mu\text{g/ml}$  for 48 h. Results showed that normal attachment, spreading and growth of B16 cells were observed for C6, C7 and C8 from a concentration of

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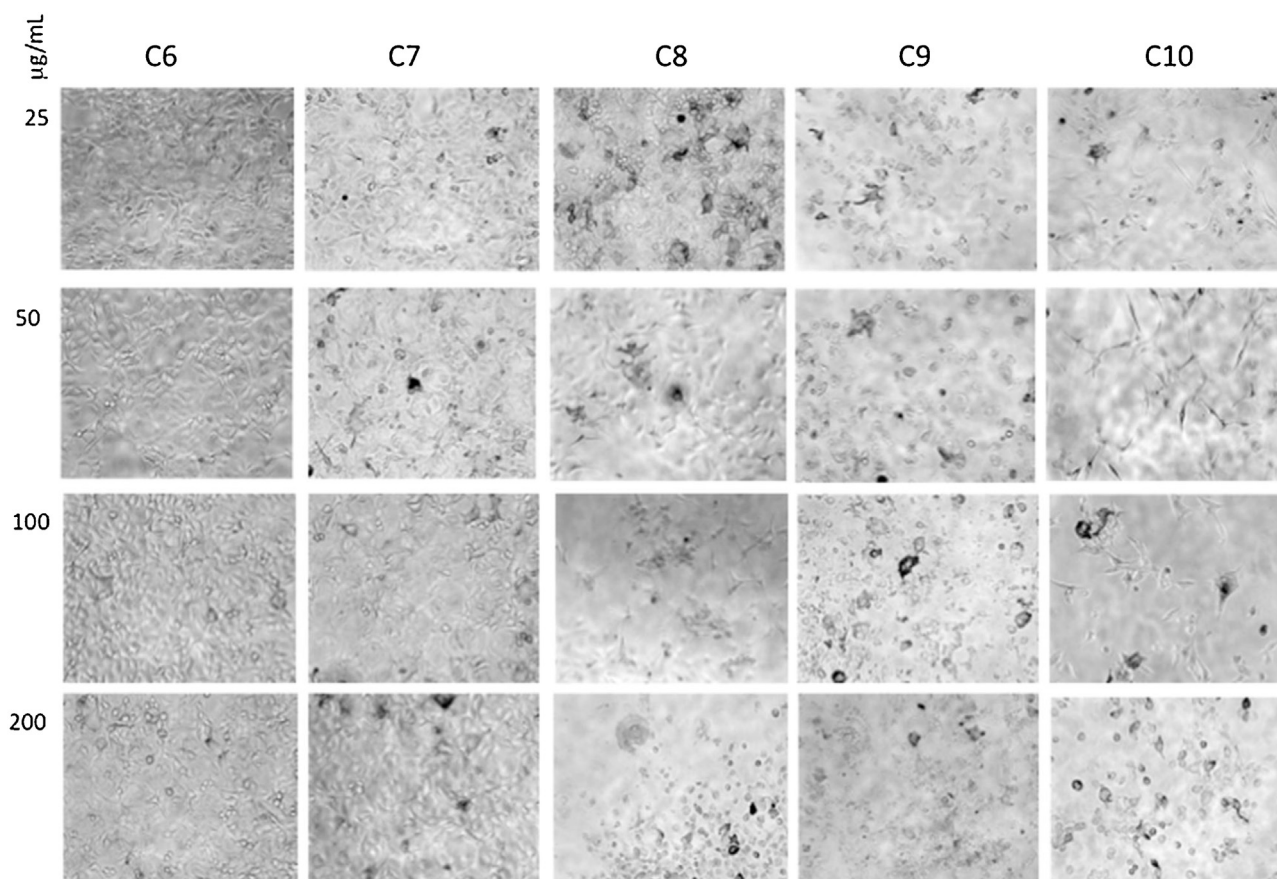


Fig. 1. Effect of perfluorocarboxylic acids on B16 cells after 48 h.

0.25  $\mu\text{g/ml}$  up to 200, 100 and 50  $\mu\text{g/ml}$ , respectively. As shown in Fig. 1, cell morphology was not affected. The viability was high at 93–97% as shown in Fig. 2, indicating that these perfluorocarboxylic acids did not have harmful effects on cells. Hence, B16 cells are relatively safe in the presence of C6, C7 and C8 within the respective concentration ranges. On the other hand, C9 and C10 exhibited moderate cytotoxicity even at a relatively low concentration of 25  $\mu\text{g/ml}$ . The cells were rounded and detached from the solid substrate. Concentrations higher than 1 mg/ml are cytotoxic (viability less than 50%) regardless of the kind of perfluorocarboxylic acid used.

Based on results, a correlation between the perfluoroalkyl chain length and cytotoxicity could be derived. Administration of the same concentration of perfluorocarboxylic acids showed a certain pattern of behavior in cells. For example, in the presence of 100  $\mu\text{g/ml}$ , viability (%) decreased with increasing perfluoroalkyl chain length C6 (97%), C7 (93%), C8 (70%), C9 (54%), C10 (50%) as shown in Fig. 2. Moreover, cell attachment to substrate and spreading decreased with increasing chain length at the same concentration. These results suggest that long-chained perfluorocarboxylic acids are more cytotoxic than short-chained perfluorocarboxylic acids. Cytotoxicity increases with increasing chain length.

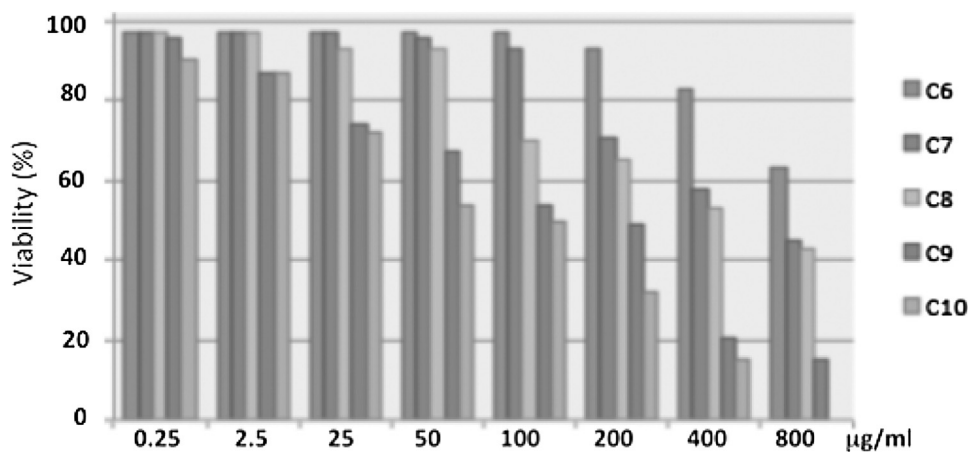


Fig. 2. Viability of B16 cells after 48 h in perfluorocarboxylic acids.

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