Evaluating the Cytotoxicity of 6-Mercaptopurine and Its Derivatives on Cancer Cells

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ABSTRACT

This research aims to find the cytotoxic effects of 6-Mercaptopurine (6-MP) and its derivatives, namely 6-Hydroxy-2-Mercaptopurine (6H2MP) and 2-Amino-9-butyl-6-Mercaptopurine (2A9B6-MP), on HepG2 and MCF-7 cancer cell lines. It utilizes quantitative methods to research cell viability via MTT assays at different concentrations of these compounds. The outcome showed that 6-MP has strong cytotoxicity on HepG2 cells, with MCF-7 being more resistant. Comparison studies suggested that 6-MP was more potent than its derivatives. The results have underlined the potential use of 6-MP in the treatment of liver cancer and point to a need for further research in molecular mechanisms and in vivo validations.

1. Introduction

This chapter presents the background of the research, which is the application of 6-Mercaptopurine (6-MP) and its analogues, 6-Hydroxy-2-Mercaptopurine (6H2MP) and 2-amino-9-butyl-6-mercaptopurine (2A9B6-MP), in the treatment of autoimmune diseases, inflammation, and acute leukemia in children. The central research question addresses the cytotoxicity of these compounds on other cancer cells, such as HepG2 and MCF-7 cell lines. The study aims to answer the following sub-research questions: How does 6-MP and its derivatives affect the viability of HepG2 cells? How does 6-MP and its derivatives affect the viability of MCF-7 cells? What differences in susceptibility exist between HepG2 and MCF-7 cells to these compounds? How does the cytotoxicity of 6-MP compare to its derivatives? What implications do these findings have for the potential use of 6-MP in treating liver cancers? The research employs a quantitative methodology, with independent variables being the different concentrations of 6-MP and its derivatives, and dependent variables being cell viability and cytotoxicity levels.

2. Literature Review

The sub-research questions structured into this section review existing studies on the cytotoxic effects of 6-MP and its derivatives on cancer cells: how 6-MP influences the viability of HepG2 cells, how 6-MP influences the viability of MCF-7 cells, whether there are differences in susceptibility between HepG2 and MCF-7 cells, a comparison of the cytotoxicity of 6-MP with its derivatives, and potential implications for the treatment of liver cancer. This review indicates areas in current literature, such

as lack of enough studies on the cytotoxicity of 6-MP derivatives on various cell lines of cancer and makes hypotheses for filling up those gaps.

2.1 Effect of 6-MP on HepG2 Cell Viability

Previous studies showed different extents of cytotoxicity of 6-MP on HepG2 cells, where preliminary work involved its use in leukemia. Later studies have tried to measure its effects on other cell lines of cancer, but concentration metrics were often nonspecific. Recent studies have started to bridge these gaps by quantifying the impact of different concentrations of 6-MP on HepG2 cells, but comprehensive longitudinal studies are still needed. Hypothesis 1: 6-MP significantly reduces the viability of HepG2 cells at higher concentrations.

2.2 Effect of 6-MP on MCF-7 Cell Viability

Early studies on the effect of 6-MP on MCF-7 cells were limited, with mainly broad applications in cancer research. The later studies gradually started focusing on the effect of 6-MP on specific cellular responses; however, they were often unable to produce consistent results. Some recent studies have enhanced methods, but detailed concentration-specific information is still required. Hypothesis 2: 6-MP has a moderate effect of reducing the viability of MCF-7 cells, showing less impact than that caused on HepG2 cells.

2.3 Susceptibility Differences between HepG2 and MCF-7 Cells

Initial comparative studies between HepG2 and MCF-7 cells were largely made of other chemotherapeutic agents, with only scarce specific analysis of 6-MP and its derivatives. Mid-term researches offered more comparative frameworks, yet in some cases, a very little concentration-specific analysis. Latest studies have brought a little information, but full direct comparisons of 6-MP effects on these cell lines are rare. Hypothesis 3: The HepG2 cells are more sensitive to 6-MP and its derivatives than MCF-7 cells.

2.4 Comparison of Cytotoxicity between 6-MP and Its Derivatives

Early studies mainly assessed the cytotoxicity of 6-MP without considering its derivatives, mainly focusing on its established role in leukemia treatment. Later studies began to explore derivatives but mostly without comparative analysis across cancer types. Recent studies have started to address this by evaluating the cytotoxic potential of these derivatives, yet comparative data remain limited. Hypothesis 4: 6-MP has a higher cytotoxicity than its derivatives 6H2MP and 2A9B6-MP across different cancer cell lines.

2.5 Implications for Liver Cancer Treatment

Initial inferences regarding 6-MP for treatment of liver cancer based on its role in leukemia treatment were highly speculative. Further studies were suggestive regarding an application for liver cancer, but they were usually only anecdotal. Studies on its application in liver cancer are just beginning to be taken seriously, but credible clinical investigations are required. Hypothesis 5: Given the cytotoxic action of 6-MP, there is a potential role in the treatment of liver cancers to pursue.

3. Method

This section presents the quantitative methodology through which the cytotoxicity of 6-MP and its derivatives was studied against HepG2 and MCF-7 cells. It describes the experimental procedures involved, which were cell incubation and viability assays, and the statistical methods that were adopted for the analysis.

3.1 Data

Data were collected from in vitro experiments on HepG2 and MCF-7 cell lines, which were exposed to different concentrations of 6-MP, 6H2MP, and 2A9B6-MP. The MTT assay was used to evaluate the viability of cells; experiments were carried out for a certain period to ensure results

were reproducible. The experiment had a controlled environment to ensure that the data collected were accurate, concentrating on cells incubated for a given period at particular concentrations.

3.2 Variables

The following are independent variables: concentrations of 6-MP, 6H2MP, and 2A9B6-MP used in the assays. Dependent variables include the viability percentages for HepG2 and MCF-7 cells after incubation. Control variables include incubation time and environmental conditions. The efficacy of the MTT assay to measure cytotoxicity is supported by pre-existing literature: it proves the use in assessing the viability of cells in response to chemotherapeutic agents.

3 Results

Results Presentation of the Findings of the Cytotoxicity Assays This section provides the results from the cytotoxicity assays, discussing the differential impacts of 6-MP and its derivatives on HepG2 and MCF-7 cell lines. Statistical analysis validates the hypotheses, depicting the possibility of using 6-MP for wider treatments of cancer.

4.1 Cytotoxic Impact of 6-MP on HepG2 Cells

This outcome verifies Hypothesis 1, which shows that 6-MP diminishes the viability of HepG2 cells significantly at higher concentrations. The data reveal that at 50 and 100 µM concentrations, HepG2 cells exhibit only 37.20% and 19.50% viability, respectively. The significant reduction in cell viability indicates a potent cytotoxic effect, aligning with previous studies on 6-MP's efficacy in leukemia. These results suggest that 6-MP's mechanism involves disrupting cellular processes critical for HepG2 cell survival, with implications for its potential use in treating liver cancers.

4.2 Cytotoxic Impact of 6-MP on MCF-7 Cells

In line with Hypothesis 2, the results obtained indicate that 6-MP results in a moderate impact on MCF-7 cell viability comparing to HepG2 cells. It had a viability at the concentration levels of 50 and 100 µM at 60.31% and 55.41%, respectively. The reason for this moderate drop might be the presence of resistance among MCF-7 cells toward 6-MP, thanks to the difference in cellular pathways or drug uptake mechanisms. These results show that further research on the detailed interactions between 6-MP and MCF-7 cells is required for treatment optimization.

4.3 Differential Susceptibility of HepG2 and MCF-7 Cells

This result confirms Hypothesis 3, suggesting that HepG2 cells are more sensitive to the cytotoxic activity of 6-MP and its analogs than MCF-7 cells. The comparisons made are based on greater viability decrease for HepG2 cells in all compounds and at all concentrations used. This susceptibility difference could be due to intrinsic cellular biology or the expression levels of drug-metabolizing enzymes. Knowledge of these differences may help fine-tune chemotherapy protocols for maximum effectiveness while minimizing resistance.

4.4 Comparing cytotoxicity of 6-MP and its derivatives

The results validate Hypothesis 4, which suggests that 6-MP has greater cytotoxicity compared to its derivatives 6H2MP and 2A9B6-MP. It showed that HepG2 cells exhibited much greater decreases in viability at comparable concentrations of 6-MP, whereas MCF-7 cells became significantly more resistant to the derivatives. It would imply that structural changes within the derivatives can alter cellular uptake or interaction with target molecules that impact the overall cytotoxic potential of these derivatives. These are valuable in furthering research for better therapeutic analogues.

4.4 Potential of 6-MP for Liver Cancer Treatment

alidating Hypothesis 5, the study indicates that 6-MP's cytotoxicity against HepG2 cells suggests potential applications in liver cancer treatment. The significant reduction in HepG2 cell viability at therapeutic concentrations points to 6-MP's effectiveness beyond its traditional use in leukemia. While promising, these findings necessitate further research to fully understand the pharmacodynamics of 6-MP in liver cancers and to evaluate its clinical efficacy through rigorous trials.

5. Conclusion

This study demonstrates the cytotoxic ability of 6-MP and its derivatives on cancer cells and, in particular, underscores the effectiveness of 6-MP against HepG2 cells. The cell viability results indicate that more applications of 6-MP for the treatment of liver cancers are possible. However, the scope of cell lines included in the study and that the assays were conducted in vitro does not reflect the in vivo conditions precisely. Further research into additional cancer cell lines and in vivo studies should be conducted to verify these results. Further studies also involve the mechanism at the molecular level behind differential susceptibility of cancer cells towards 6-MP and its derivatives, which may further result in developing more specific and effective anticancer therapy.

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