

Abstract

# Formulation of Pullulan Acetate Nanoparticles Loaded with 5-fluorouracil †

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**Introduction:** The aim of this study was to obtain and characterize pullulan acetate-based nanoparticles, loaded with an anticancer agent, 5-fluorouracil (5-FU). The 5-FU agent is a first-line chemotherapeutic agent, employed in the treatment of various types of cancer, such as: gastric, pancreatic and esophageal cancer, breast cancer, head and neck cancer, cervical cancer, kidney cancer, etc. However, 5-FU has a short biological half-life, non-selective distribution, variable oral bioavailability and toxicity, which limits its therapeutic applicability. A way to overcome these limitations is by loading 5-FU in nanoparticles [1–3]. **Materials and Methods:** Pullulan was produced through a fermentation process, by *Aureobasidium pullulans* strain, and was further chemically modified with dimethylformamide, pyridine and acetic anhydride to obtain pullulan acetate. The 5-FU-loaded pullulan acetate nanoparticles were obtained by various methods: nanoprecipitation method, modified nanoprecipitation method and double emulsion method. Nanoparticles were characterized in terms of entrapment efficiency, size and polydispersity index, using spectrophotometric and dynamic light scattering techniques. **Results:** The 5-FU-loaded pullulan acetate nanoparticles were successfully produced by the three methods (nanoprecipitation, modified nanoprecipitation and double emulsion). All samples showed nanometric size and narrow polydispersity index. **Conclusions:** This study shows that pullulan and its derivatives have a great potential for the production of nanoparticles, with application in the biomedical field, including for the delivery of anticancer agents, as 5-fluorouracil.

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## References

1. Schirmacher, V. From chemotherapy to biological therapy: A review of novel concepts to reduce the side effects of systemic cancer treatment. *Int. J. Oncol.* **2019**, *54*, 407–419. [[PubMed](#)]
2. Huang, L.; Chaurasiya, B.; Wu, D.; Wang, H.; Du, Y.; Tu, J.; Webster, T.; Sun, C. Versatile redox-sensitive pullulan nanoparticles for enhanced liver targeting and efficient cancer therapy. *Nanomed. Nanotechnol. Biol. Med.* **2018**, *14*, 1005–1017. [[CrossRef](#)] [[PubMed](#)]
3. Hossen, S.; Hossain, K.; Basher, M.K.; Mia, M.N.H.; Rahman, M.T.; Jalal Uddind, M. Smart nanocarrier-based drug delivery systems for cancer therapy and toxicity studies: A review. *J. Adv. Res.* **2019**, *15*, 1–18. [[CrossRef](#)] [[PubMed](#)]