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AVHANDLINGENS *Impact of pharmaceutical formulation on physico-*
TITTEL: *chemical and in vitro photobiological properties of*
porphyrin photosensitizers

'Porfyriner, som brukes i fotodynamisk terapi av kreft viser lav løselighet i vann, noe som begrenser deres terapeutiske effekt. Målet for dette prosjektet var å lage nanopartikler som solubilisierer utvalgte porfiriner og undersøke egenskapene avgjørende for deres potensiale som legemiddelbærere. Doktorgradsarbeidet danner et godt grunnlag for videre utvikling av slike nanopartikler for bedre behandlingseffekt og reduserte bivirkninger.'

There is a need to develop novel modalities for therapy of various cancers and to enhance current therapies in order to ensure a more efficient treatment with fewer side effects. Photodynamic therapy of cancer utilizes non-toxic compounds, *i.e.* photosensitizers, that exert antineoplastic action upon activation by a concentrated beam of red laser light. However, many photosensitizers are characterized by low aqueous solubility, which limits their therapeutic potential. Solubilization and encapsulation of photosensitizers into tailor-made nano-sized carriers composed of micelle-forming copolymers, *e.g.* Plurionics®, may be used to overcome this issue. These nanoparticles may also prove useful in targeting the drugs to the desired location in the body, subsequently reducing side effects.

The goal of this thesis was to identify key structural properties of porphyrin photosensitizers and Plurionics that influence the process of solubilization and encapsulation. An aim was to identify the variables important to maintain beneficial pharmaceutical properties and high antineoplastic activity as well as to ensure the thermodynamic stability of the formulation.

The photosensitizer-Pluronic nanoparticles were characterized by measurements of size, morphology and surface charge. The interactions between selected porphyrin photosensitizers and different Pluronic assemblies (*i.e.* single Pluronic molecules and nano-sized micelles) were investigated in various media. The antineoplastic activity of selected porphyrin photosensitizers encapsulated in nano-sized copolymeric micelles towards cancer monolayer cultures was measured and compared to plain photosensitizer solutions. Uptake of photosensitizers into the cancer cells was observed and quantified by use of microscopic techniques.

Aqueous solubility and light absorption properties of the photosensitizers, necessary for their photochemical activation, were increased upon encapsulation by Pluronic nanocarriers. Consequently, it was possible to enhance antineoplastic activity of some photosensitizers by selecting a proper nanomicellar formulation. Concluding, nano-sized copolymeric micelles can be used as carriers for porphyrin photosensitizers, considering an optimal Pluronic type is utilized. This doctoral research forms a good basis for further development of such nanocarriers for improved photodynamic therapy of cancer.

