

Our results provide basis for further applied research, *e.g.* developing new antimicrobial peptides in therapy, pest control and food preservation.

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Opening of the blood-brain barrier for drug delivery to the brain: the effects of temmilifene and short-chain alkylglycerols on brain endothelial cells

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The blood-brain barrier (BBB) forms a dynamic interface between the blood and the brain. It selectively regulates the transcellular and paracellular transport of molecules and passage of cells between the blood and the central nervous system. The BBB restricts drug penetration to the brain preventing effective treatment of several neurological diseases. Therefore it is an increasing need to find new ways to improve drug delivery to the brain. Brain capillary endothelial cells constitute the anatomical and functional basis of the BBB. One of the strategies to increase drug delivery to the brain is changing cerebral endothelial functions by opening the BBB through the modification of the paracellular or the transendothelial transport pathways.

In this study two agents, temmilifene and short-chain alkylglycerols (AGs) were selected for detailed examination. Temmilifene, a tamoxifen-related compound, has chemopotentiating properties in experimental and in clinical cancer studies. Treatment with temmilifene caused temporary, acute CNS side-effects in patients indicating the opening of the BBB. Previous studies from our laboratory have shown that temmilifene increases the permeability of the BBB in rats. Intraarterial injection of short-chain AGs, such as 1-*O*-pentylglycerol and 2-*O*-hexyldiglycerol, open the BBB and increase the delivery of molecules to rodent brain parenchyma *in vivo*. The mechanism underlying AG and temmilifene-mediated modification of BBB permeability is still unknown. The aim of the present study was to test the direct effects of temmilifene and AGs on barrier properties of cultured brain microvascular endothelial cells, a model of the BBB.

The triple co-culture BBB model was constructed on cell culture inserts using primary rat brain endothelial cells, rat cerebral glial cells and rat pericytes. Barrier integrity of the BBB endothelial monolayers was analyzed by transendothelial electrical resistance and permeability measurements. In addition to functional assays, toxicity tests, immunostainings for junctional proteins and freeze fracture electron microscopy were performed.

Short-term temmilifene and AG treatment decreased the resistance of endothelial monolayers, and increased the permeability for fluorescein, a marker of paracellular flux. Temmilifene also enhanced the transcellular transport of albumin. These short-term changes were accompanied by changes in cell morphology and immunostaining for junctional proteins. AG and temmilifene-mediated increase in brain endothelial permeability was reversible. Short-term treatments did not alter the viability of brain endothelial cells. Temmilifene did not affect the functions of P-glycoprotein, but decreased the activity of the multidrug resistance associated protein-1 and the production of nitric oxide in endothelial cells. Temmilifene also altered the mRNA expression of several tight junction proteins measured by a custom Taqman gene array.

Our data support previous clinical observations and the results of animal experiments, and clearly indicate that AGs and temmilifene increase the permeability of the BBB by directly acting on brain endothelial cell functions. Temmilifene and AGs are promising adjuvants in the transient opening of the BBB for clinical use, especially for treatment of brain tumors.

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Metagenomics of biogas producing microorganisms

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The production of renewable energy carriers is currently receiving increasing attention worldwide. Biogas is a promising technology as its production may combine the treatment of various organic wastes with the generation of energy. Biogas can be converted to heat and/or electricity, and its purified derivative, biomethane, is suitable for every function for which fossil natural gas is used today. The degradation