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Hydraulic stimulation of geothermal reservoirs: fluid flow, electric potential and microseismicity

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Description

The drug salinomycin (SAL) is a polyether antibiotic and used in veterinary medicine as coccidiostat and growth promoter. Recently, SAL was suggested as a potential anticancer drug. However, transformation products (TPs) resulting from metabolic and environmental degradation of SAL are incompletely known and structural information is missing. In this study, we therefore systematically investigated the formation and identification of SAL derived TPs using electrochemistry (EC) in an electrochemical reactor and rat and human liver microsome incubation (RLM and HLM) as TP generating methods. Liquid chromatography (LC) coupled to high-resolution mass spectrometry (HRMS) was applied to determine accurate masses in a suspected target analysis to identify TPs and to deduce occurring modification reactions of derived TPs. A total of 14 new, structurally different TPs were found (two EC-TPs, five RLM-TPs, and 11 HLM-TPs). The main modification reactions are decarbonylation for EC-TPs and oxidation (hydroxylation) for RLM/HLM-TPs. Of particular interest are potassium-based TPs identified after liver microsome incubation because these might have been overlooked or declared as oxidated sodium adducts in previous, non-HRMS-based studies due to the small mass difference between K and O + Na of 21 mDa. The MS fragmentation pattern of TPs was used to predict the position of identified modifications in the SAL molecule. The obtained knowledge regarding transformation reactions and novel TPs of SAL will contribute to elucidate SAL-metabolites with regards to structural prediction. Salinomycin (SAL) is an ionophore antibiotic that shows antibacterial, antifungal, antiparasitic, and antiviral properties. SAL is commercially used as a veterinary drug to treat and prevent coccidiosis in poultry farming. Furthermore, SAL shows potential as growth promoter in modern animal husbandry (usage not allowed in the EU). In 2009, Gupta et al. observed that SAL selectively negatively impacts on breast cancer stem cells, inducing intensive studies of SAL as a novel therapeutic agent in different human cancer types (e.g., breast, colon, and leukemia). The chemical structure of SAL consists of a polyether skeleton with five polyether rings. Three rings form a unique tricyclic spiroketal system, whereby the middle ether ring has a double bond. Similar to other ionophore antibiotics, SAL has a carboxylic group and an ether-ring with a hydroxy-group in terminal positions. These specific structural properties lead to the occurrence of a pseudo cyclic SAL complex with metal cations

The Advantage of the Surface Geophysical Methods

In flat coastal areas, near-surface geophysical techniques have been widely used in groundwater research to acquire this basic information. Geophysical techniques are high-resolution tools that provide information on the spatial distribution of the physical parameters of the subsoil. These techniques are non-invasive and become useful when lithological data are sparse or not able to provide detailed subsurface information required for groundwater modeling. The advantage of the surface geophysical methods, compared with borehole methods, is that they allow denser and faster data coverage at a much lower cost, reduce risks to interconnect different water bodies during drilling operations, and can provide a way to improve the subsurface characterization from a set of boreholes. Adult (postnatal) fibroblast-like CD73CD90CD105+ AMSCs cultivated on plastic wells in a StemPro® Differentiation Kit (Thermo Fisher Scientific, USA) for 21 days were positively stained with alizarin red S (osteoblasts), alcian blue (chondrocytes), and oil red (adipocytes) and compared with unstained cells in standard medium. The findings showed that the cells met the morphological criteria of multipotent MSCs (MMSCs) as described in PEO (molecular weight (MW) ≈ 600,000 g/mol) and PVA (MW ≈ 89000-98000 g/mol and 99+% hydrolyzed) powders were purchased from Sigma-Aldrich, USA. Vulcan XC72R carbon black was generously donated by Cobat inc. These reasonably high MW materials are appropriate to prepare polymer blends owing to their film forming charac- teristics. Different thicknesses of stencil sheets were utilized to create the desired micro- structures. Glass was utilized as a substrate. DI water was used as a solvent.

Chloride channels are a functionally and structurally diverse group of selective channels, associated with cell volume and regulation and excitability in cardiac, neuronal, and smooth muscle cells. Due to their relationship with cell volume regulation, they are interesting targets to inhibit cancer cell motility (BR J Pharmacol, 2009). ClC-2 and ClC-3 are Cl− channels that are identified to be specifically upregulated in the membranes of gliomas cells. Increased expression of these channels endow glioma cells with an enhanced route of Cl−

transport; in turn facilitating changes in cell shape and size during division and invasion. A study utilising a gene expression array data set (accession number: GSE3289) identified 18 ion channel genes that are differentially expressed as prognostic molecular subtypes. Of the 18 channel genes identified, 16 were down regulated in HGG including the epithelial sodium channel SCN1A, anion channel VDAC, potassium channel KCNJ10 and the purinoreceptor P2RX7. However, the chloride channels CLIC1 and CLI4 were both upregulated in the high-grade cohort. A second microarray data set was employed to validate these findings (accession number: GSE4290) and the results were mirrored. Kaplan Meyer testing confirmed that tumours that harboured this 18 gene ion channel signature were associated with decreased overall survival in the cohorts compared to tumours with ion channel signature.

A growth inhibition assay was performed against the gram positive bacteria Staphylococcus aureus (ATCC 29213) and Bacillus cereus (ATCC 11778) and two gram negative bacteria Pseudomonas aeroginosa (ATCC 27853) and Salmonella Typhimurium (ATCC 14028) using the Kirby-Bauer disc diffusion method. Solutions of the compounds were prepared in distilled water with concentration of 100 mg/mL. 10 µL of these sample solutions were pipetted onto the discs and allowed to incubate at 37°C for 24 hours. The activities of the compounds were determined by measuring the diameter of the zone of inhibition in mm. CTAB which is commonly use as an antiseptic was used as a positive control using the same concentration of the tested compounds. The study shows that the synthesised N, N, N-triethyl ammonium phenylalanine esters have potential antibacterial actitvities against both gram positive and gram negative bacteria. They display better activity compared to the phenylalanine ester hydrochloride. This shows that the quaternary ammonium moiety have better interactions with the bacterial cell membrane.