

Salinomycin

Salinomycin is an antibacterial and coccidiostat ionophore therapeutic drug.

1 Antibacterial activity

Salinomycin and its derivatives exhibit high antimicrobial activity against Gram-positive bacteria, including the most problematic bacteria strains such as methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-resistant *Staphylococcus epidermidis* (MRSE), and *Mycobacterium tuberculosis*. Salinomycin is inactive against fungi such as *Candida* and Gram-negative bacteria.^[1]

2 Cancer research

2.1 Pre-clinical

Salinomycin has been shown by Piyush Gupta et al. of the Massachusetts Institute of Technology and the Broad Institute to kill breast cancer stem cells in mice at least 100 times more effectively than the anti-cancer drug paclitaxel. The study screened 16,000 different chemical compounds and found that only a small subset, including salinomycin and etoposide, targeted cancer stem cells responsible for metastasis and relapse.^{[2][3][4][5]}

The mechanism of action by which salinomycin kills cancer stem cells specifically remains unknown, but is thought to be due to its action as a potassium ionophore due to the detection of nigericin in the same compound screen. Studies performed in 2011 showed that salinomycin could induce apoptosis of human cancer cells. Promising results from a few clinical pilot studies reveal that salinomycin is able to effectively eliminate CSCs and to induce partial clinical regression of heavily pretreated and therapy-resistant cancers. The ability of salinomycin to kill both CSCs and therapy-resistant cancer cells may define the compound as a novel and an effective anti-cancer drug.^{[6][7]} It has been also shown that Salinomycin and its derivatives exhibit potent antiproliferative activity against the drug-resistant cancer cell lines.^{[8][9]} Salinomycin is the key compound in the pharmaceutical company Verastem's efforts to produce an anti-cancer-stem-cell drug.

3 Use in agriculture

Salinomycin is used in chicken fodder as a coccidiostat.

4 Biosynthesis

A team from the University of Cambridge has cloned and sequenced the biosynthetic cluster responsible for salinomycin production, from *Streptomyces albus* DSM 41398.^[10] This has shown that the polyketide backbone of salinomycin is synthesised on an assembly line of nine polyketide synthase (PKS) multienzymes. Furthermore, the cluster contains genes involved in oxidative cyclization including *salC* (epoxidase) and *salBI/BII/BIII* (epoxide hydrolase) genes. The cluster also contains genes suspected to be involved in self-resistance, export, precursor supply and regulation. Interestingly, the cluster contains a NRPS-like carrier protein, SalX, that is suspected to tether "pre-salinomycin" during oxidative cyclization. By inactivating *salC* the Cambridge-based team have demonstrated that salinomycin biosynthesis proceeds via a diene intermediate.

5 See also

- Narasin a derivative of salinomycin which has an additional methyl group.
- Targeted therapy

6 References

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