

Title: **Trabectedin: example of a marine alkaloid with antineoplastic activity. Origin, isolation, structure, synthesis and mechanism of action**

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The first living beings appeared in the marine ecosystem more than 3500 million years ago and their evolutionary development has allowed them to improve their mechanisms for survival. The marine ecosystem is one of the most important sources of many complex structures and bioactive compounds, and is believed to be a source for drug discovery in the future. Cancer is a disease that affects a large part of the world's population and is therefore one of the most important health problems today. The discovery of new drugs of natural origin (as is the case with Trabectedin) has emerged as a potential pathway in search of anti-cancer drugs. Safety in the use of natural products for the drug discovery process is based on the fact that they contain bioactive molecules that are developed to bind with molecules within the biological system, making them suitable as therapeutic agents. Trabectedin is an antitumour drug obtained from ascidia *Ecteinascidia turbinata*. It is a tetrahydroisoquinolinic alkaloid containing a cysteine residue and seven chiral centers. The drug exerts its activity on tumor cells through its interaction with the transcription complex and blocking DNA repair. YONDELIS® (trabectedin) is approved in nearly 80 countries in Europe, North America, Asia and South America for the treatment of advanced single-agent soft tissue sarcoma and for recurrent and platinum-sensitive ovarian cancer in combination with DOXIL®/CAELYX® (pegylated liposomal doxorubicin). In July 2007, European Medicines Agency (EMA) allowed Trabectedin to be marketed and became the first natural compound from the sea for the treatment of cancer. It is currently synthesized by a semisynthesis process from an antibiotic (cyanosafrafracin B) obtained from the fermentation of the bacteria *Pseudomonas fluorescens*. The chemical interactions of the compound interfere with various transcription factors, DNA binding proteins and DNA repair pathways. PharmaMar is the Spanish company based in Madrid that markets Yondelis in Europe. It is an innovative company in the research of drugs that come from the marine ecosystem. The company also has an agreement with Johnson & Johnson to market the drug outside Europe.

Keywords: ("bioactive compound", "therapeutic agents", "tetrahydroisoquinolinic alkaloid", "chiral centre" , "transcription complex" , "sarcoma", "semisynthesis" , "anti-tumour activity" , "tumour microenvironment").