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Differential Inhibitory Effects of Cytotoxic Agents on Lymphoma Cell Proliferation and Tumor Growth Salicylanilides and their Anticancer Properties

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Abstract

Lymphoma is a cancerous tumour that develops from the lymphatic hematopoietic system. Although it is more likely to occur in lymph nodes, it can invade almost any tissues and organs in the body due to lymphatic system flow, making treatment ineffective, particularly in non-Hodgkin lymphoma. Tumor targeted therapy has received a lot of attention in recent years. Drugs that target tumour cells can precisely attack tumours while causing minimal damage to normal cells. As demonstrated in the research of antibody-drug conjugate (ADC), small molecules should have a suitable half maximal inhibitory concentration (IC50) value as a key aspect of tumour targeted drugs, so the selection of small molecules is critical and also challenging for drug development.

Throughout the long history of antitumor research, many active ingredients extracted from plants and microorganisms have demonstrated potent antitumor activity. Microtubules (MTs), which play an important role in mitosis, are frequently used as cancer therapy targets [1]. Ansamitocin P3 is a maytansine analogue discovered in Nocardia species. It has been shown to disrupt microtubule assembly by binding to tubulin at the same site as vinblastine. Following ansamitocin P3 treatment, cells were arrested in the mitotic phase and apoptosis was induced. Despite its high cytotoxicity, ansamitocin P3 has not been approved for clinical use due to severe side effects and a limited therapeutic spectrum.

Anticancer Properties of Salicylanilides

Salicylanilides are biologically active compounds with a diverse range of effects. Halogenated salicylanilides, which have been used as anthelmintics in human and veterinary medicine for decades, have recently emerged as drug repurposing candidates in oncology. The most well-known salicylanilide anthelmintic being studied for its potential anticancer properties is niclosamide [2]. Nonetheless, recent research has revealed that a number of other salicylanilides have significant anticancer potential. In the field of anticancer therapy, there is an ongoing need to find new, effective drugs. A modern trend is the effort to develop drugs with highly selective activity against tumour cells and lower toxicity than conventional antitumor therapy.

The development of new anticancer drugs is a complex process with one of the highest attrition rates when compared to other drug groups [3]. One appealing strategy for overcoming the difficulties associated with drug development in oncology is drug repurposing (that could be also called drug repositioning, reprofiling or re-tasking). This strategy seeks new medical applications for previously approved or investigational drugs in different indications. Because of the existing information on the safety profile of already registered drugs, this approach is especially advantageous and can significantly reduce development costs and timelines. Drugs from the salicylanilide group, formed by the union of a salicylic acid and an aniline, are among the promising candidates for oncology repurposing.

Paclitaxel, another molecule isolated from the Pacific yew tree Taxus brevifolia, is a widely used cancer treatment. As a microtubule-stabilizing agent, it can cause chromosome non-segregation, mitotic arrest, and cell apoptosis. Paclitaxel has been approved by the FDA for the treatment of many types of tumours since it was first approved for the treatment of ovarian and breast cancer [4]. However, the high toxicity and low solubility of paclitaxel make it unsuitable as a drug candidate; thus, nanotechnology was developed to improve the solubility and safety of paclitaxel.

Camptothecin (CPT), a pentacyclic alkaloid derived from Camptotheca acuminata, also has antitumor properties and has been used in tumour therapy for decades. It is a Topo inhibitor that can disrupt DNA replication and cause apoptosis. Since 1994, irinotecan, a camptothecin-derived drug, has been approved for the treatment of several advanced cancers [5]. However, owing to its high toxicity and poor solubility, camptothecin's use was also restricted. Many biomolecules show great potential for development as targeted antitumor drugs as biomolecule conjugation technology and tumour targeting therapy advance . We compared the antitumor effects of ansamitocin P3, paclitaxel, and camptothecin on lymphoma U937 cells, investigated potential apoptosis mechanisms, and investigated the inhibition effect of ansamitocin P3 in the xenograft tumour model in order to identify appropriate therapeutic molecules suitable for targeting lymphoma or other cancer cells.

Materials and Procedures

Cell culture and cell lines

Histolytic lymphoma in humans U937 cells were obtained from the Chinese Academy of Sciences' Shanghai Cell Bank and cultured

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in RPMI-1640 medium supplemented with 10% foetal bovine serum and 1% penicillin-streptomycin; all of these reagents were provided by Gibco (Thermo Fisher Scientific). Cells were incubated at 37°C and kept in a 5% CO2 environment [6].

Chemicals

Ansamitocin P3 (purity > 98%), paclitaxel (purity 99.97%) and camptothecin (purity 99.69%) were purchased from MCE (Med Chem Express, NJ, USA). PBS, RNase A was obtained from Solarbio (Solarbio Life Science, Beijing, China). Matrigel basement membrane matrix was supplied by BD Biosciences.

Cell cycle examination

Cells were seeded into six-well plates at a density of 2 105 cells per well and treated with various drug concentrations for 24 hours. Cells were collected and washed with PBS before being fixed in 70% ethanol at -20°C for several hours to days before being centrifuged at 4000 rpm for 2 minutes. Cell pellets were then resuspended in 500 l of PBS containing 0.25% Triton-X 100 and incubated for 15 minutes on ice [7]. The cells were then resuspended in 500 l PBS with 10 g/ml RNase A and 20 g/ml PI and incubated in the dark at room temperature for 30 minutes.

An examination of apoptosis

Cells were seeded into six-well plates at 2 105 cells per well for apoptosis analysis and treated for 48 hours with ansamitocin P3, camptothecin, and paclitaxel at various concentrations. After being collected and washed with PBS, cells were suspended in 100 l binding buffer and incubated for 15 minutes with 5 l FITC-AV and 5 l PI (binding buffer, FITC-AV, and PI were supplied with the detection kit). Finally, samples were detected on the flow cytometer after 400 l of binding buffer was added.

The granular endoplasmic reticulum has the appearance of a simplified structure. Amorphous, granular of filamentous material can accumulate in the cisternae. Fragmentation and degranulation are frequently found, with the interruption of connections between the granular endoplasmic reticulum and mitochondria. Fingerprint like formations are not uncommon. The decrease of the granular endoplasmic reticulum from tumor cells occurs concomitantly with an increase of free ribosomes and polysomes, which shows an enhanced production of proteins necessary for the cell growth process.

During the initiation phase, the agranular endoplasmic reticulum is hyperplastic without being associated with functional hyperactivity. The endoplasmic reticulum is reduced in other stages of cancer [8-10].

The Golgi apparatus is generally underdeveloped in malignant cells, which has a positive correlation with tumour cell differentiation. Cells that have lost all differentiation occasionally show a Golgi apparatus. Mitochondria shrink in volume as tumours grow. Mitochondria vary greatly in shape and volume, and massive mitochondria have been observed on occasion. The "Warburg phenomenon" refers to abnormal glycolysis processes that occur in mitochondrial membranes. Changes in mitochondrial crystals occur, as do inclusions in the matrix and the appearance of pyknotic images. A cytochrome oxidase deficiency is involved in the longitudinal distribution of mitochondria.

Peroxisomes are only found in tumours formed by cells that normally contain these organelles, such as hepatocytes. It has been established that the number of peroxisomes produced by malignant cells is inversely proportional to pace of growth and expresses the degree of differentiation loss. Glycogen in high concentrations is a hallmark of cancer, particularly in the liver and kidneys, but malignant cells generally contain a small amount of glycogen, as seen in hepatic and cervical carcinomas. The decrease of glycogen until its dissolution parallels the increase of lipids. Lysosomes change because of cell malignancy. As a result, secondary lysosomes, myelinic structures, and lipofuscin granules appear.

Conclusion

Cytoplasmic inclusions can manifest degenerative cellular changes. Apoptosis occurs in some types of neoplasms, with the presence of apoptotic bodies. Malignant cells contain varying amounts of microfilaments, intermediate filaments, and microtubules. The ability of a cancerous tissue to invade and metastasize is dependent on its ability to move, which is ensured by the actin content. Cytokeratins are found in epithelial carcinomas, vimentin in mesenchymal tumours , and an acid protein from glial fibres in central nervous system cells, which plays a special role in tumour diagnosis.

References

1. Zondervan KT, Becker CM, Koga K, Missmer SA, Taylor RN, et al. (2018) Endometriosis Nat Rev Dis Primers 4:9.
2. Stephansson O, Falconer H, Ludvigsson JF (2011) Risk of endometriosis in 11,000 women with celiac disease. Hum Reprod 26:2896-2901.
3. Selam B, Kayisli UA, Garcia-Velasco JA, Arici A (2002) Extracellular matrix-dependent regulation of Fas ligand expression in human endometrial stromal cells. Biol Reprod 66:1-5.
4. Sampson JA (1927)Peritoneal endometriosis due to the menstrual dissemination of endometrial tissue into the peritoneal cavity. Am J Obstet Gynecol 14:422–469.
5. Poppe K, Velkeniers B (2003) Thyroid disorders in infertile women. Ann Endocrinol 64:45-50.
6. May KE, Conduit-Hulbert SA, Villar J, Kirtley S, Kennedy SH, et al. (2010) Peripheral biomarkers of endometriosis: a systematic review. Hum Reprod Update 16:651–674.
7. Lee KK, Jharap B, Maser EA, Colombel JF (2016) Impact of concomitant endometriosis on phenotype and natural history of inflammatory bowel disease. Inflamm Bowel Dis 22:159-163.
8. Liu E, Nisenblat V, Farquhar C, Fraser I, Bossuyt PM, et al. (2015) Urinary biomarkers for the non-invasive diagnosis of endometriosis. Cochrane Database Syst Rev 23:12.
9. Matorras R, Ocerin I, Unamuno M, Nieto A, Peiro E, et al. (2007) Prevalence of endometriosis in women with systemic lupus erythematosus and Sjögren's syndrome. Lupus 16:736-740.
10. Healey M, Cheng C, Kaur H (2014) To excise or ablate endometriosis? A prospective randomized double-blinded trial after 5-year follow-up. J Minim Invasive Gynecol 21:999-1004.