

Advances in the Pharmacological Effects and Molecular Mechanisms of Dulcitol and Its Derivatives

Quan QUAN, Junhao LI, Xichun HUANG, Zhao NING, Hongye LI, Wenhui ZHAO, Chenghao JIN*

College of Life Science and Biotechnology, Heilongjiang Bayi Agricultural University, Daqing 163319, China

Abstract Through a comprehensive review of both domestic and international literature, the pharmacological effects and molecular mechanisms of dulcitol and its derivatives have been systematically summarized. The findings demonstrate that dianhydrogalactitol (DAG) and diacetyldianhydrogalactitol (DADAG) induce apoptosis in tumor cells, inhibit angiogenesis, and arrest the cell cycle via mitochondrial, death receptor, and endoplasmic reticulum stress pathways. Additionally, dulcitol mitigates intestinal inflammation and barrier damage by inhibiting the TLR4/MyD88/NF- κ B signaling pathway, while also modulating intestinal microbiota and promoting defecation. Collectively, dulcitol and its derivatives exhibit multi-target pharmacological activities, indicating their promising potential in the prevention and treatment of cancer and intestinal disorders.

Key words Dulcitol, Dianhydrogalactitol (DAG), Diacetyldianhydrogalactitol (DADAG), Pharmacological effect, Molecular mechanism

1 Introduction

Dulcitol, also referred to as galactitol, is a naturally occurring hexahydric alcohol commonly found in plants belonging to the Celastraceae family (such as *Gymnosporia confertiflora* and *Euonymus fortunei*), as well as in seaweeds and various other higher plants^[1]. Its molecular formula is $C_6H_{14}O_6$, and it has a molecular weight of 182.17 g/mol. At room temperature, dulcitol appears as a white crystalline powder that is readily soluble in water and exhibits a melting point ranging from 187 to 190 °C. Modern pharmacological research demonstrate that dulcitol exhibits a range of biological activities. However, initial studies primarily concentrated on the synthesis of its derivatives, including dianhydrogalactitol (DAG) and diacetyldianhydrogalactitol (DADAG), which have been investigated as antitumor agents^[2–3].

Tumors, particularly malignant ones, represent a significant threat to global public health. According to the World Health Organization, cancer is the second leading cause of death worldwide, with both incidence and mortality rates rising annually. The clinical management of malignant tumors is challenged by factors such as difficulties in early diagnosis, high rates of recurrence and metastasis, and the development of drug resistance during treatment. Therefore, it is of considerable clinical importance to identify highly effective and low-toxicity anti-tumor agents and to elucidate their mechanisms of action. Dulcitol derivatives, such as DAG and DADAG, are compounds that exhibit significant anti-tumor

activity^[2–4]. Their mechanisms of action include the induction of tumor cell apoptosis, inhibition of angiogenesis, arrest of cell cycle, *etc.*

2 Pharmacological effects and its molecular mechanisms

2.1 Anti-tumor mechanism

2.1.1 Mechanism of inducing apoptosis in tumor cells. Numerous studies have demonstrated that DAG and its derivatives can induce apoptosis in tumor cells via multiple pathways. Su Guiyu *et al.*^[5] investigated the inhibitory effect of DAG on the proliferation of 11 human lung cancer cell lines *in vitro* using the CCK-8 assay. Their results indicated that DAG exerted a significant concentration-dependent inhibitory effect on cell lines including Calu-1, NCI-H1650, and A549. Transmission electron microscopy analysis demonstrated that the cells exhibited characteristic apoptotic morphological features, including overall shrinkage, microvilli shedding, nuclear condensation and margination, mitochondrial swelling, and the formation of intracellular vacuoles. Quantitative real-time fluorescence PCR results indicated that DAG upregulated the expression of the pro-apoptotic protein Bax, downregulated the expression of the anti-apoptotic protein Bcl-2, and activated Caspase-3. These findings suggest that DAG induces tumor cell apoptosis via the mitochondrial apoptotic pathway. Zhang Yuling *et al.*^[6] examined the effects of dulcitol on C6 glioma cells. Their findings demonstrated that dulcitol significantly inhibited the proliferation of C6 cells, exhibiting a clear concentration-dependent effect. Hoechst staining revealed nuclear condensation within the cells. Furthermore, Western blot analysis confirmed that the mechanism underlying dulcitol-induced apoptosis in glioma cells was closely associated with the regulation of the Bax/Bcl-2 ratio.

Zhou Ying *et al.*^[7–8] investigated the *in vivo* anti-tumor effects of DAG by establishing a nude mouse model bearing human non-small cell lung cancer H460 cell xenografts. The results dem-

Received: March 5, 2026 Accepted: June 26, 2026

Supported by Central Government Funds for Local University Reform and Development (2020GSP16); Undergraduate Innovation and Entrepreneurship Training Program of Heilongjiang Province (202510223002); Postgraduate Innovation Research Project of Heilongjiang Bayi Agricultural University (YJSCX2025-KJQN66, YJSCX2025-XCZX84).

Quan QUAN, master's degree candidate, research fields: pharmacology of anti-cancer drugs. * Corresponding author. Chenghao JIN, doctoral degree, professor, research fields: pathogenesis of cancer and drug development.

onstrated that the tumor inhibition rate of DAG at all tested doses exceeded 40%, accompanied by a significant increase in tumor cell apoptosis. RT-qPCR and Western blot analyses revealed that DAG upregulated the mRNA and protein expression levels of Bax, Caspase-3, Caspase-9, and P53, while downregulating Bcl-2 expression. These findings further confirm that DAG exerts its anti-tumor effects via the mitochondrial apoptotic pathway. Jiang Xia *et al.*^[9] demonstrated that DAG significantly inhibited the proliferation of human glioma cell lines U251 and BT325 in a dose- and time-dependent manner. Using laser confocal microscopy, the study revealed that DAG reduced the mitochondrial membrane potential, elevated intracellular Ca^{2+} concentration, and concurrently induced DNA damage in these cells. Further mechanism investigations indicated that DAG upregulated the mRNA expression of genes associated with the death receptor pathway, including *Caspase-8* and *Fas*, as well as genes related to the endoplasmic reticulum stress pathway, such as *Caspase-4*, *CHOP*, *GRP78*, and *GRP94*. These findings suggest that DAG modulates apoptosis and proliferation in glioma cells through both the death receptor and endoplasmic reticulum stress pathways. Huang Yinmei *et al.*^[10–11] investigated the inhibitory effects of DAG on the proliferation of lung cancer NCI-H460 cells using the CCK-8 assay and colony formation assay. Their results demonstrated that DAG consistently suppressed tumor cell proliferation. Hoechst staining revealed significant chromatin alterations within the cell nuclei, while single-cell gel electrophoresis indicated that DAG induced DNA damage. Fluo-3 AM fluorescence staining showed an elevation in intracellular Ca^{2+} concentration, and Rhodamine 123 staining revealed a reduction in mitochondrial membrane potential. Real-time PCR and Western blot analyses demonstrated that DAG decreased both the mRNA transcription levels and protein expression of Topo II α and Topo II β . Furthermore, molecular docking simulations suggested that DAG bound to Topo II, implying that DAG inhibits Topo II activity, leading to double-strand DNA breaks and subsequent tumor cell death.

2.1.2 Mechanisms of angiogenesis inhibition. Tumor angiogenesis plays a critical role in tumor growth and metastasis. Consequently, inhibiting angiogenesis has emerged as a significant strategy in anti-tumor therapy. Jiang Xia *et al.*^[9] investigated the effects of DAG on the migratory and invasive capabilities of human glioma cells through scratch assays and Transwell migration and invasion assays. Their findings demonstrated that DAG inhibited cell migration, invasion, and *in vitro* angiogenesis in a dose- and time-dependent manner. Furthermore, ELISA results indicated that DAG significantly reduced the levels of VEGF and FGF-2 in the supernatant of glioma cells. Mechanism studies revealed that DAG upregulated PTEN expression while downregulating MMP-2 expression, thereby suppressing tumor cell invasion and migration. Wang Xiaojie *et al.*^[12] investigated the effects of DAG on human umbilical vein endothelial cells (HUVECs). The MTT assay results indicated that DAG inhibited HUVEC proliferation in a

manner dependent on both concentration and exposure duration. Additionally, the scratch assay, Transwell migration assay, and Matrigel tube formation assay collectively demonstrated that DAG suppressed the migratory capacity and lumen formation of HUVECs. Findings from RT-PCR, ELISA, immunohistochemistry, and Western blot analyses further confirmed that DAG downregulated the expression of pro-angiogenic factors, including VEGFA, VEGFR-2, FGF-2, MMP-2, and MMP-9. Subsequent validation using a zebrafish model revealed that DAG inhibited the development of inferior mesenteric veins in zebrafish embryos and reduced mRNA transcription levels of VEGFAA, VEGFR-2, FGF-2, and FGFR-2, thereby substantiating the anti-angiogenic properties of DAG. Liu Jingtao *et al.*^[13] investigated the inhibitory effects of DADAG on tumor growth and angiogenesis using a mouse H22 model. Their findings demonstrated that DADAG administered at doses of 5 and 10 mg/kg $\cdot$ d significantly reduced tumor weight, with inhibition rates of 29.8% and 60.2%, respectively, as well as microvessel density, with inhibition rates of 38.9% and 66.7%, respectively, in a dose-dependent manner. Additionally, DADAG induced tumor tissue necrosis, decreased the expression levels of VEGF and Sp1, and exhibited no apparent hepatorenal toxicity. These results suggest that the antitumor effects of DADAG are closely associated with its capacity to inhibit angiogenesis.

2.1.3 Mechanisms of cell cycle arrest. DAG and its derivatives have been shown to inhibit tumor growth by arresting the cell cycle in tumor cells. Liang Qiaofang *et al.*^[14] investigated the *in vitro* inhibitory effects of DAG on 11 human brain tumor cell lines using the MTT assay. The results demonstrated that the 72 h IC_{50} values for cell lines including IMR-32, SH-SY5Y, U87, A172, BT325, T98G, SHG-44, U373, C6, SK-N-BE, and U251 ranged from 19.24 to 25.13 $\mu\text{g/mL}$. These findings suggest that DAG exerts a broad-spectrum growth inhibitory effect on human brain tumor cells. Zhang Huiling *et al.*^[15–16] reported that the 72 h IC_{50} values of DAG against H460, SGC-7901, BEL-7404, and SMMC-7721 tumor cell lines were 15.98, 16.00, 16.73, and 16.46 $\mu\text{g/mL}$, respectively, indicating broad-spectrum antitumor activity. Yan Xuelian *et al.*^[17] examined the effects of DADAG on the proliferation of human prostate cancer PC-3M cells. Sulforhodamine B (SRB) assay results demonstrated that treatment with 40 mg/L DADAG for 48 and 72 h inhibited cell proliferation by 34.6% and 47.8%, respectively. Cell cycle analysis revealed that exposure to 5, 10, and 20 mg/L DADAG for 48 h increased the proportion of cells in the G_2/M phase to 47.4%, 62.9%, and 69.1%, respectively. Western blot analysis indicated that DADAG downregulated the expression of Cdc25C while upregulating Cyclin B1, p-Cdc2 (Tyr15), and Wee1. These findings suggest that DADAG induces cell cycle arrest in G_2/M phase, potentially through modulation of key cell cycle regulatory proteins.

In conclusion, the dulcitol derivatives DAG and DADAG exhibit significant anti-tumor activities. Their mechanisms of action encompass multiple pathways, including the induction of tumor

cell apoptosis via the mitochondrial pathway, death receptor pathway, and endoplasmic reticulum stress pathway; inhibition of angiogenesis through downregulation of the VEGF/VEGFR-2 signaling pathway and suppression of vascular endothelial cell function; and inhibition of tumor cell proliferation and migration by regulating the cell cycle and inhibiting Topo II activity. These findings indicate that DAG and DADAG hold considerable potential for the development of novel anti-tumor agents.

2.2 Anti-inflammation and intestinal protection The intestinal barrier serves as the primary defense mechanism against the invasion of external pathogens, and its integrity is essential for maintaining intestinal homeostasis. Weaning stress can damage the tight junctions of the intestinal epithelium in piglets, leading to intestinal inflammation and diarrhea. Impairment of intestinal epithelial barrier function is closely associated with inflammatory responses, with the Toll-like receptor 4 (TLR4)/myeloid differentiation factor 88 (MyD88)/nuclear factor- κ B (NF- κ B) signaling pathway playing a pivotal regulatory role in these inflammatory processes. Dulcitol has demonstrated potential therapeutic value in mitigating intestinal barrier damage and inflammatory responses, owing to its biological activities, including modulation of the intestinal microbiota and anti-inflammatory effects.

Wang Han *et al.* [18] conducted a study using weaned piglets and porcine intestinal epithelial cells (IPEC-J2) to systematically investigate the mitigating effects of dulcitol on LPS-induced intestinal barrier injury and inflammatory responses. The results from animal experiments demonstrated that dietary supplementation with 500 mg/kg dulcitol significantly increased final body weight, average daily gain, and average daily feed intake in weaned piglets, while reducing the feed-to-gain ratio. Compared to the LPS group, dulcitol administration significantly enhanced serum SOD activity and decreased the levels of MDA, IL-1 β , and TNF- α . Additionally, dulcitol improved intestinal morphology by increasing jejunal villus height, the villus-to-crypt ratio, and the number of goblet cells in colonic crypts, and also upregulated the expression of barrier proteins, including ZO-1, CLDN-1, OCLN, and MUC2 in the colonic mucosa. Furthermore, dulcitol treatment inhibited the expression of inflammation-related proteins in the colonic mucosa, such as TLR4, MyD88, I κ B- α , and IL-1 β , significantly reducing the p-NF- κ B/NF- κ B ratio. These findings indicate that dulcitol alleviates intestinal inflammation by suppressing the TLR4/MyD88/NF- κ B signaling pathway. Cellular experiments further confirmed the protective effects of dulcitol. When IPEC-J2 cells were pretreated with 200 μ mol/L dulcitol, this pretreatment significantly enhanced cell viability, migration distance, and migration area compared to the LPS-treated group. Additionally, it increased the expression of the anti-apoptotic protein Bcl-2 while markedly decreasing the levels of the pro-apoptotic protein Bax and the autophagy-related protein Beclin1. Dulcitol pretreatment also significantly upregulated the expression of barrier-associated proteins, including ZO-1, OCLN, CLDN1, and MUC2. In con-

trast, the expression of inflammation-related proteins such as TLR4, MyD88, I κ B- α , NF- κ B, and IL-1 β was significantly reduced. Multi-omics sequencing analysis revealed that dulcitol treatment significantly increased the abundance of *Lactobacillus* and *Blautia* in the colonic mucosa, while significantly decreasing the abundance of Proteobacteria. *Lactobacillus* and *Blautia* exhibited significant positive correlations with SOD, OCLN, and CLDN. Additionally, *Blautia* demonstrated significant negative correlations with I κ B- α , MyD88, and the p-NF- κ B/NF- κ B ratio. Proteomic analysis identified 240 differentially expressed proteins predominantly enriched in pathways associated with lysosome, cell cycle regulation, fatty acid metabolism, and alcoholic liver disease. Among these, the differentially expressed proteins CADM1 and IRAK4, which are implicated in intestinal barrier function, immune response, and inflammation, showed significant negative correlations with MDA, MyD88, and p-NF- κ B/NF- κ B, as well as significant positive correlations with OCLN. Wang Han *et al.* [19] conducted a study elucidating the molecular mechanisms by which dulcitol mitigated LPS-induced injury in IPEC-J2 cells. The study identified 200 μ mol/L dulcitol as the optimal treatment concentration and 150 μ g/mL LPS as the effective pro-inflammatory dose. The findings demonstrated that dulcitol pretreatment alleviated the reduction in cell density, the formation of vacuoles, and indistinct cell boundaries, while significantly enhancing cell migration distance and area. Furthermore, dulcitol pretreatment markedly upregulated the mRNA transcription and protein expression levels of barrier-associated genes, including *ZO-1*, *OCLN*, and *CLDN1*, as well as the mRNA levels of *MUC2*, *LATS1*, and *YAPI*. Concurrently, dulcitol pretreatment significantly downregulated the mRNA transcription and protein expression levels of pathway-related genes such as *MyD88*, *I κ B- α* , *NF- κ B*, *IL-1 β* , the protein expression of *TLR4*, and the mRNA transcription levels of *NLRP3* and *IL-18*. The aforementioned results demonstrate that dulcitol mitigates LPS-induced intestinal barrier damage and inflammatory responses by downregulating the expression of proteins associated with the TLR4/MyD88/NF- κ B signaling pathway and modulating the secretion of inflammatory factors.

In conclusion, dulcitol inhibits inflammatory responses by modulating the TLR4/MyD88/NF- κ B signaling pathway, thereby conferring protective effects on the intestinal barrier and renal function. Consequently, dulcitol holds potential for development as a novel feed additive or organ-protective pharmaceutical agent.

2.3 Other pharmacological effects and mechanisms

2.3.1 Antioxidant mechanism. Zhai Chunqing *et al.* [20] employed bioinformatics analysis and zymosan-activated serum (ZAS) to induce podocyte injury, thereby establishing both a cellular injury model and a membranous nephropathy rat model. Their study investigated the mechanism by which dulcitol ameliorated membranous nephropathy through modulation of the peroxisome proliferator-activated receptor α (PPARA)/ATP-binding cassette transporter A1 (ABCA1) signaling pathway. The findings

demonstrate that PPARA serves as a critical target of dulcitol in treating membranous nephropathy. Overexpression of dulcitol or PPARA mitigated ZAS-induced oxidative stress in podocytes, with dulcitol exhibiting a superior effect. Conversely, knockdown of ABCA1 exacerbated oxidative stress. Furthermore, dulcitol improved renal function in rats and upregulated the expression of PPARA and ABCA1. These results suggest that dulcitol inhibits oxidative stress and ameliorates membranous nephropathy by activating the PPARA/ABCA1 signaling pathway, thereby broadening its potential applications in renal protection.

2.3.2 Regulation of intestinal microbiota and enhancement of defecation mechanisms. He Pei *et al.* [21] investigated the role of dulcitol in modulating human intestinal flora using a functional assessment method. In the test, 51 volunteers were randomly assigned to either a trial diet group or a control group. The trial group consumed 2 g of dulcitol daily for 30 consecutive days. The results demonstrated a significant increase in *Lactobacillus* amount within the trial group before and after the intervention ($P < 0.01$). Furthermore, the *Lactobacillus* amount in the trial group was significantly higher than that in the control group following the trial ($P < 0.01$). These findings suggest that daily intake of 2 g dulcitol effectively regulates human intestinal flora by promoting probiotic activity without adversely affecting the physical health of the participants. Wang Diankui *et al.* [22] conducted a randomized double-blind study involving 52 patients with constipation, who were assigned to either a trial diet group or a placebo control group. The trial group received 2 g of dulcitol daily for 14 consecutive days. The results demonstrated that, compared to the control group, the trial group exhibited a significant increase in defecation frequency ($P < 0.05$), as well as improvements in defecation conditions and fecal consistency ($P < 0.05$). Intra-group comparisons revealed that the trial group experienced a significant increase in defecation frequency ($P < 0.01$) and improvements in both defecation conditions and fecal consistency ($P < 0.05$). The findings suggest that daily intake of 2 g of dulcitol exerts a laxative effect without adverse impacts on the physical health of the participants.

3 Prospects

Dulcitol and its derivatives, as a class of natural small-molecule compounds exhibiting diverse pharmacological activities, have demonstrated considerable potential in applications such as anti-tumor, anti-inflammatory, intestinal protection, modulation of intestinal microbiota, and regulation of defecation. In recent years, significant progress has been achieved in the study of dulcitol and its derivatives, but several limitations and challenges remain. Firstly, the majority of existing research has concentrated on the anti-tumor properties of dulcitol derivatives (*e. g.*, DAG and DADAG), whereas investigations into the pharmacological effects of dulcitol itself remain comparatively limited. Secondly, although existing studies have demonstrated that dulcitol possesses functions such as protecting the intestinal barrier and modulating the intesti-

nal microbiota, its molecular mechanisms remain to be fully elucidated. In particular, the detailed regulatory mechanisms underlying its interactions with the intestinal microbiota warrant further investigation. Thirdly, research on the target sites of dulcitol and its derivatives remains incomplete. Existing studies have demonstrated that it exerts effects via multiple pathways, including the mitochondrial apoptotic pathway, the death receptor pathway, the endoplasmic reticulum stress pathway, the TLR4/MyD88/NF- κ B signaling pathway, and the PPARA/ABCA1 signaling pathway. However, its direct molecular target remains unidentified, which constrains efforts in targeted structural optimization and the development of novel therapeutics. Fourthly, the *in vivo* pharmacokinetic investigations of dulcitol and its derivatives remain insufficient. Although prior research has demonstrated that DAG can traverse the blood-brain barrier, comprehensive pharmacokinetic parameters, including absorption, distribution, metabolism, and excretion, have yet to be fully elucidated, thereby limiting the precision of their clinical application [23]. Fifthly, the safety assessment of dulcitol and its derivatives requires further enhancement. Studies utilizing zebrafish models have indicated that high concentrations of DAG exhibit neurodevelopmental toxicity [24–25], underscoring the necessity to carefully consider the safety window during drug development. It is imperative to delineate the relationship between therapeutic and toxic doses to establish a foundation for the rational clinical use of these compounds.

In conclusion, dulcitol and its derivatives exhibit multi-target and multi-pathway pharmacological properties, demonstrating distinct advantages in areas such as anti-tumor activity and the prevention and treatment of intestinal diseases. With ongoing research elucidating their mechanisms of action and continuous advancements in dosage form development, dulcitol is anticipated to assume an increasingly significant role in clinical applications.

References

- [1] TANG RJ, DENG Q, BI NJ. Extraction and content determination of dulcitol[J]. Chinese Pharmaceutical Journal, 1984(11): 57. (in Chinese).
- [2] Wei Kang Chun (dianhydrogalactitol)[J]. Chinese Pharmaceutical Journal, 1986(3): 158–159. (in Chinese).
- [3] TAO RF, LIN BJ. A new anticancer drug: Dianhydrogalactitol[J]. New Drugs and Clinical Remedies, 1985(4): 248. (in Chinese).
- [4] SHEN YJ, DENG N, DING H, *et al.* Progress in the study of antitumor effects of 1,2:5,6-Dianhydrogalactitol and diacetyldianhydrogalactitol[J]. Journal of Tianjin University of Traditional Chinese Medicine, 2021, 40(5): 653–658. (in Chinese).
- [5] SU GY, LIU HG, HUANG HX, *et al.* *In vitro* anticancer activity and mechanisms of 1,2:5,6-dianhydrogalactitol on human lung cancer cell lines[J]. Chinese Journal of Experimental Traditional Medical Formulae, 2016, 22(10): 122–127. (in Chinese).
- [6] ZHANG YL, ZHANG T, CHEN BG, *et al.* *In vitro* antitumor activity of dulcitol on C6 glioma cells and related mechanism[J]. Hunan Journal of Traditional Chinese Medicine, 2024, 40(2): 168–172, 200. (in Chinese).

- [7] ZHOU Y, LIU HG, SUN YW, *et al.* Anti-cancer effect of 1,2 : 5,6-dianhydrogalactitol on human non-small cell lung cancer H460 and its mechanism[J]. Journal of Guangxi Medical University, 2022, 39(2) : 215 – 220. (in Chinese).
- [8] ZHOU Y. Anti-tumor effects and mechanism of 1,2 : 5,6-dianhydrogalactitol on tumor innude mice transplanted human lung cancer cell H460[D]. Nanning: Guangxi Medical University, 2016. (in Chinese).
- [9] JIANG X. Effects and mechanism of dianhydrogalactitol on proliferation, apoptosis, invasion and angiogenesis of human glioma cells[D]. Nanning: Guangxi Medical University, 2016. (in Chinese).
- [10] HUANG YM. Effect of dianhydrogalactitol on lung cancer NCI-H460 cells and its antitumor mechanism based on topoisomerase II[D]. Nanning: Guangxi Medical University, 2017. (in Chinese).
- [11] HUANG YM, LIU HG, SU GY, *et al.* Inhibitory effect of dianhydrogalactitol on DNA TopoII in NCI-H460 cells[J]. Chinese Pharmacological Bulletin, 2016, 32(11) : 1601 – 1607. (in Chinese).
- [12] WANG XJ. THE Experimental study of dag on angiogenesis[D]. Nanning: Guangxi Medical University, 2016. (in Chinese).
- [13] LIU JT, GUO W, XU B, *et al.* Inhibitory effect of diacetyldianhydrogalactitol on tumor growth and angiogenesis of mouse transplanted liver cancer H22[J]. Chinese Journal of New Drugs, 2011, 20(2) : 115 – 119. (in Chinese).
- [14] LIANG QF, LIU HG, TAN Q, *et al.* Inhibitory effect of 1,2 : 5,6-Dianhydrogalactitol on human brain tumor cells *in vitro* [J]. Guangxi Sciences, 2015, 22(4) : 454 – 456. (in Chinese).
- [15] ZHANG HL. *In vitro* antitumor effect of dianhydrogalactitol and its apoptosis induction on hepatoma cell SMMC-7721[D]. Nanning: Guangxi Medical University, 2013. (in Chinese).
- [16] ZHANG HL, WANG JN, LIANG S, *et al.* Inhibitory effect of 1,2 : 5, 6 dianhydrogalactitol on four different kinds of tumor cells *in vitro* [J]. Guangxi Sciences, 2013, 20(1) : 82 – 84. (in Chinese).
- [17] YAN XL, XU B, LI M, *et al.* Inhibition of diacetyldianhydrogalactitol on ornithine decarboxylase activity and its possible mechanisms [J]. Chinese Pharmaceutical Journal, 2009, 44(12) : 904 – 908. (in Chinese).
- [18] WANG H. Dulcitol alleviates LPS-induced intestinal barrier damage and inflammatory response in weaned piglets[D]. Yangling: Northwest A&F University, 2024. (in Chinese).
- [19] WANG H, LIU ZQ, ZHU LB, *et al.* Dulcitol alleviates lipopolysaccharide induced porcine small intestinal epithelial cells injury by modulating toll-like receptor 4/myeloid differentiation factor 88/nuclear factor- κ B signaling pathway[J]. Chinese Journal of Animal Nutrition, 2024, 36(6) : 3952 – 3962. (in Chinese).
- [20] ZHAI CQ, PEI M, WEN N. Dulcitol ameliorates membranous nephropathy by activating the PPARA/ABCA1 signaling pathway to inhibit oxidative stress[J/OL]. Journal of China Medical University, 1 – 8[2026 – 04 – 02]. (in Chinese).
- [21] HE P, MA YH, LIU RM, *et al.* Study on the regulation effect of dulcitol on human intestinal flora[J]. Heilongjiang Science, 2021, 12(4) : 28 – 31. (in Chinese).
- [22] WANG DK, MA YH, LIU RM. Human experimental study of dulcitol defecation[J]. Heilongjiang Science, 2021, 12(2) : 18 – 21. (in Chinese).
- [23] YANG JN. Antitumor effect and molecular mechanism of diacetyldianhydrogalactitol[R]. Journal of Xinxiang Medical University, 2004 – 12 – 02. (in Chinese).
- [24] PENG XL, CAO W, LI C, *et al.* Evaluation of neurodevelopmental toxicity of dianhydrogalactitol in zebrafish[J]. Chinese Journal of Modern Applied Pharmacy, 2023, 40(15) : 2093 – 2099. (in Chinese).
- [25] PENG XL, LIU HG, SU GY, *et al.* Safety evaluation of dianhydrogalactitol to zebrafish embryos[J]. Chinese Journal of Experimental Traditional Medical Formulae, 2016, 22(6) : 134 – 139. (in Chinese).

(From page 24)

- [2] LIANG WJ, LIU J, SONG LY. Construction of ideological and political construction system of environmental courses in colleges and universities [J]. China Modern Educational Equipment, 2023 (23) : 109 – 110, 113. (in Chinese).
- [3] LU DK. The researches on and difficulties in ideological and political education in the new era and its prospects[J]. Journal of Xinjiang Normal University(Philosophy and Social Sciences), 2022, 43(3) : 43 – 58. (in Chinese).
- [4] ZHANG DL. Curriculum ideological and political education: The fundamental guideline for fostering virtue through education in the new era[J]. China Higher Education Research, 2021(1) : 5 – 9. (in Chinese).
- [5] CHEN H, XUE G, MA CY, *et al.* Exploration of cultivating innovative

talents in environmental engineering through the connotation of curriculum ideological and political education [J]. Journal of Higher Education, 2025, 11(13) : 74 – 77. (in Chinese).

- [6] LU HJ, WENG XL, LOU LP, *et al.* Exploration and practice of curriculum ideological and political education in environmental engineering based on course groups[J]. Journal of Higher Education, 2026, 12(8) : 44 – 48. (in Chinese).
- [7] ZHOU Y, ZHOU Q, GAO R. Analysis of "three grips" for curriculum ideological and political construction in practical courses: Based on the practice of environmental innovation and entrepreneurship courses [J]. The Party Building and Ideological Education in School, 2023(1) : 80 – 82. (in Chinese).

(From page 33)

- [10] BAO XZ, YU XC, NIU ZS, *et al.* Effects of aianthone on endogenous AR and related factors in prostate cancer 22RV1 cells[J]. Northwest Pharmaceutical Journal, 2022, 37(2) : 62 – 66. (in Chinese).
- [11] HE YD. Function and mechanism of natural small molecule aianthone in inhibiting the growth and metastasis of castration-resistant prostate cancer[D]. Shanghai: East China Normal University, 2014. (in Chinese).

- [12] GUO J. Effect of aianthone on cell proliferation, cell cycle and apoptosis of human nasopharyngeal carcinoma CNE-2 cells[D]. Nanning: Guangxi Medical University, 2019. (in Chinese).
- [13] WANG SH, CHEN QX, CHEN XY, *et al.* Aianthone inhibits cell proliferation in tongue squamous cell carcinoma via PI3K/AKT pathway [J]. Evidence-Based Complementary and Alternative Medicine, 2022 : 3859489.