Anticancer Potential of Diazepam: Pharmacological Relevance and Clinical Evidence

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Abstract: Cancer treatments such as chemotherapy, radiation, and targeted therapies often face challenges like severe side effects, drug resistance, and high costs. Repurposing existing medications is a promising strategy to improve treatment outcomes. Diazepam (DZP), a benzodiazepine commonly used for anxiety, has recently shown potential anticancer effects. This study explores the anticancer activity of DZP, focusing on its mechanisms of action, pharmacological relevance, immunotherapy, pharmacokinetics profile, toxicological profile, and clinical evidence through literature review from articles and journals in PubMed, Scopus, Google Scholar, and the Web of Science. DZP exerts antitumor effects by inducing apoptosis, inhibiting cell proliferation, and modulating oxidative stress and cell cycle dynamics against various cancers: blood cancer, brain cancer, breast cancer, colorectal cancer, glioblastoma, lung cancer, and skin cancer. DZP also demonstrates synergistic potential with conventional chemotherapeutic agents, enhancing their effectiveness while reducing patient anxiety and stress. Its pharmacokinetic profile, characterized by rapid absorption, extensive tissue distribution, and a prolonged half-life, supports its utility as a sustained anticancer agent. A significant gap in our investigation is the lack of clinical data on DZP; additional clinical evidence is required to validate its anticancer potential and establish it as an anticancer drug in the near future. Its sedative and CNS depressant effects necessitate cautious use, particularly in patients with hepatic or renal impairment. This review highlights the potential of DZP as a cost-effective, repurposed therapeutic option for cancer treatment. Additionally, it demonstrates how DZP may be a viable anticancer medication with a potential mechanism, maybe providing a better safety profile and less serious side effects than traditional treatments like chemotherapy.

Keywords: Cancer; Diazepam; Literature review; Pharmacological relevance

1. Introduction

Cancer continues to be a major global health challenge and a universal cause of morbidity and mortality, which attributes to about 10 million deaths in the year 2020 (Sung et al., 2021). About 20 million new cases and 9.7 million deaths were attributed to cancer worldwide as of 2022 (Bray et al., 2024). According to estimates, there would be 611,720 cancer-related fatalities and 2,001,140 new cancer cases in the US in 2024 (Siegel et al., 2024). Cancer is characterized by unregulated cell division that disrupts tissue and organ function, with malignant cells infiltrating surrounding tissues and spreading throughout the body. Common types include breast, lung, prostate, colorectal, and stomach cancers, each with distinct bio-clinical traits. Symptoms vary by type and stage but often include persistent fatigue, unexplained weight loss, pain, and skin changes (Siegel et al., 2020). Cancer remains a major global burden, with approximately 19.3 million new cases diagnosed in 2020, a number expected to rise due to aging populations and lifestyle changes (Bray et al., 2018). The high cost of treatment, loss of productivity, and its frequent coexistence with chronic diseases like diabetes and cardiovascular conditions further complicate management and add to the economic impact (Koene et al., 2016).

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However, conventional cancer treatments are primarily based on surgery, radiation therapy, and chemotherapy, with immunotherapy and targeted therapies added as backup (Chen et al., 2018). Although the chemotherapeutic agents such as doxorubicin and cisplatin, remain the mainstay of treatment; severe side effects (cardiotoxicity, nephrotoxicity, and neurotoxicity) limit their efficacy (Minotti et al., 2004; Meredith et al., 2009; Kaur et al., 2023). Furthermore, and of importance, is the increasing occurrence of drug resistance owing to reduced treatment effectiveness and disease recurrence (Holohan et al., 2013; Al Hasan et al., 2024). Cisplatin is highly effective against testicular and ovarian cancers but is nephrotoxic and neurotoxic (Florea & Büsselberg, 2011). There is therefore a need for searching for alternative therapeutic approaches to increase efficacy and decrease the risk of side effects.

Specific cancer types have shown promise for targeted therapies, including tyrosine kinase inhibitors (imatinib) and monoclonal antibodies (trastuzumab) to improve patients' outcomes (Lemmon & Schlessinger, 2010). However, these therapies are costly and tend to result in resistance over time, and thus the study of alternative or adjunctive treatment options (Hirsch et al., 2016). Consequently, novel pharmacological agents that are more effective and less toxic are urgently needed.

Benzodiazepine, such as DZP, a pharmacological agent used as an anxiolytic, muscle relaxant, and anticonvulsant, has recently gained interest for its antitumor properties (Aktar et al., 2024). We have shown in studies that DZP can regulate basic cellular processes such as apoptosis, proliferation, and angiogenesis, which are indispensable to cancer development (Sieghart & Sperk, 2002). These effects are thought to be mediated through the interaction of the albumin with $GABA_A$ receptors, mitochondrial channels, and calcium signaling pathways (Štrac et al., 2008).

A series of studies have recently shown the promise of repurposing existing drugs to treat cancer, including DZP (benzodiazepine, sold under the trade name Valium, used to treat anxiety and seizures). Inhibition of cancer cell proliferation and modulation of $GABA_A$ receptor by modulating DZP have been shown to be promising anticancer activities (Jia et al., 2016; Chowdhury et al., 2024b). Additionally, it has been attributed to effect functions regarding mitochondrial function and calcium ion channels (Chen et al., 2019). These findings suggest that DZP may be a complementary or alternative therapeutic strategy for cancer that would increase treatment dose intensity and reduce toxicity.

DZP appears to exhibit selective cytotoxic effects toward different cancer cell lines, including glioblastoma, melanoma, and breast cancer (Velázquez et al., 2020). In addition to this, its unique ability to make chemotherapy drugs more effective while lowering stress and increasing anxiety in chemo patients is a multifaceted therapeutic approach (García-Muñoz et al., 2017). However, the specific mechanisms by which these drugs work and potentially apply to the clinic still remain to be determined. DZP presents some limitations in cancer therapy, including the potential for tumor-promoting effects, drug interactions, and immune suppression. Additionally, its sedative properties and risk of dependence should be carefully considered, which highlights the importance of exploring alternative treatments with fewer side effects and greater efficacy in oncology (Szewc et al., 2022; Sneyd et al., 2021; Bhuia et al., 2025).

This literature review critically reviews studies in existence to date on the anticancer activity of DZP, covering its mechanism of action, experimental evidence, and potential clinical applications. This review attempts to synthesize current knowledge in order to inform on the possibility of this drug being repurposed as an adjunctive therapy in cancer treatment and to identify future research avenues. In addition, it underscores the necessity for complete preclinical and clinical characterization of its safety and efficacy profiles in oncology.

2. Methodology

2.1. Literature Search Strategy

The impact of DZP against cancer cells was evaluated by searching articles and journals in PubMed, Scopus, Google Scholar, and the Web of Science, which focused on pharmacological and biological topics. The following were used in the study: Diazepam OR Valium; Cancer OR Neoplasms; Anticancer activity OR Apoptosis. The aim was to find out the mechanisms, consequences, and function of diazepam in cancer therapy on cancer cells. To do this, we used research articles from earlier to more recent years and in the English language, as our study focused on findings from developed countries. Besides, we focused on only peer-reviewed journals, as they are considered to be more reliable than other types of journal articles.

2.2. Data Inclusion and Exclusion Criteria

These reviews' inclusion criteria were as follows: (a) English language; (b) peer-reviewed journal articles, clinical trials, preclinical research, and *in vitro*/*in vivo* experiments; (c) studies that explore diazepam's anticancer effects; (d) studies published after the year 2000. The exclusion criteria included non-English published articles, other drug-related studies with no special reference to diazepam, studies published in languages other than English, and studies that were based on the primary properties of the drug, i.e., anxiolytic and anticonvulsant effects, and without including anticancer properties of the drug.

3. Results and Discussion

3.1. Anticancer activity of diazepam

Cancer is a condition in which DNA abnormalities cause cells to proliferate out of control, either producing tumors or spreading to other areas of the body. It can infiltrate tissues or organs and interfere with regular cell processes (Anand et al., 2023). Generally, cells divide according to DNA instructions in an orderly manner to replace damaged or aged cells. These instructions can be disrupted by genetic mutations, and unregulated cell growth can result from damage to DNA. In addition, these mutations may be caused by random errors made during cell replication, smoking, UV radiation, illnesses, or inherited characteristics (López-Lázaro, 2018; Basu, 2018). Cancer can be described as either benign or malignant. Malignant tumors have the ability to infect neighboring tissues and metastasize to other sections of the body (Kotamkar et al., 2021). Therefore, DNA abnormalities, cell proliferation, avoiding planned cell death, metastasis, and angiogenesis are examples of general

cancer pathways (Wajed et al., 2001; Paoli et al., 2013). Anticancer compounds are therefore intended to inhibit these pathways.

Cytotoxicity assays are crucial for assessing potential drugs by figuring out how well they can destroy cancer cells while leaving healthy cells unharmed. Eliminating cancer cells with the least amount of damage to healthy cells is the aim of cancer treatment (Bhuia et al., 2024). Moreover, uncontrolled tumor cell proliferation is a hallmark of cancer, frequently brought on by mutations in proteins that control the cell cycle. Thus, focusing on cell cycle regulators is seen to be a promising strategy for creating cancer treatments (Matthews et al., 2022). Apoptosis is a type of planned cell death that helps preserve tissue homeostasis and happens in response to internal or external stimuli. Consequently, anticancer medications cause damaged or aberrant cells to undergo apoptosis and die, which stops them from growing and spreading unchecked and helps stop the development and spread of tumors (O'Brien & Kirby, 2008). The proliferation of irregular cells, frequently brought on by modifications in cell cycle-related proteins, is what propels the development and spread of cancer, making them a dependable target for anticancer medication research. So, drugs with anti-proliferative properties possess anticancer activity (Donev, 2023).

Based on a review of the literature, this study investigated the anticancer effects of DZP against different cancer types and how they responded to particular DZP therapies in both *in vitro* and *in vivo* models. In colorectal and breast cancer, using SNU-C4 and MDA-MB-231 cells treated with 10^{-5}–10^{-10} M concentrations of DZP, VEGF and GM-CSF levels decreased, and apoptosis and cell cycle arrest increased, with IC_{50} values of 5.5 ± 1.2 μM and 0.12 ± 0.1 μM, respectively (Kim et al., 2008). Breast cancer cells (MCF-7, MDA-MB-231) treated with 10^{-6} M showed reduced glucose utilization, proliferation, and PBR mRNA expression with an IC_{50} of 2.4 ± 0.3 μM (Kim et al., 2009). Glioblastoma studies (U87, GBM T98G) demonstrated increased cytotoxicity, cell cycle arrest, and decreased proliferation at EC_{50} levels (Lavička et al., 2001; Chen et al., 2013). Colorectal cancer (SNU-C4 cells) and skin cancer (B16 melanoma cells) exhibited increased cytotoxicity and apoptosis at 10^{-6} M and 75 μM concentrations, respectively (Lee et al., 2009; Landau et al., 1998). Lung cancer (V79 cells) had an IC_{50} of 106.8 ± 8.89 μM, showing increased apoptosis (Camins et al., 1995). Brain cancer and tumors, assessed via multiple assays and cell lines, revealed significant reductions in proliferation and cell cycle dynamics at IC_{50} values of 36.7 ± 5.1 μM and 175–220 ± 30 μM (Gorman et al., 1989; Laurent Miccoli et al., 1998). Additionally, blood cancer studies demonstrated enhanced apoptosis and decreased cell cycle dynamics at 0.1–1 μg/mL (Hadžiabdić et al., 2017). **Table 1** shows the anticancer database findings from several pieces of literature. The molecular anticancer mechanisms are summarized in **Fig. 1**.

Therefore, based on existing research, it is evident that DZP may benefit patients with aggressive tumors like glioblastoma, lung, and breast cancer, particularly those with dysregulated cell cycles and high oxidative stress. DZP has anticancer effects by eliciting apoptosis, cell cycle arrest, cytotoxicity, inhibition of proliferation, mRNA expression, cell survival, and other anticancer mechanisms. DZP may therefore be a therapeutic alternative for the treatment of cancer; however, further preclinical and clinical research must be prioritized.

3.2. Immunotherapy

Immunotherapy is the process of boosting the body's natural defense system, providing a more focused and maybe less harmful option. It has also changed the way that cancer is treated (Ghulam & Iqbal, 2024). We found some studies on the immunotherapeutic use of DZP. DZP counteracts the immunostimulatory action of anti-ACBP/DBI neutralization in a mouse model of cancer chemoimmunotherapy (Montégut et al., 2024). DZP was also used to treat the symptoms of NMDAR encephalitis in conjunction with first- and second-line immunotherapy, frequently at its greatest dosage during active treatment stages (Shin et al., 2021). Another study shows that treatment with DZP affects dendritic cell activity, reduces inflammation and neurodegeneration in experimental autoimmune encephalomyelitis (EAE), and affects the innate immune system both *in vitro* and *in vivo* (Falcón et al., 2021; Chowdhury et al., 2024a). These findings suggest that although DZP is mainly used to treat symptoms, new research shows that it may also be used as an immunotherapeutic agent. Its function in immune regulation may be better understood, and its therapeutic indications may be expanded with more research.

3.3. Pharmacological relevance

The present review is focused on the possible anticancer effects of DZP, a benzodiazepine primarily used to treat anxiety disorders, seizures, and to induce sleep. The present study showed that DZP potentially possesses anticancer effects due to changes in various cellular activities like the presence of oxidative stress, cell cycle disruption, and apoptotic effects. The authorized intrinsic apoptotic pathway has been proved to induce cancer cell apoptosis through overexpression of pro-apoptotic proteins such as caspases and BAX (Ke et al., 2017). Also, DZP has an antiproliferative effect and acts on the cell cycle, changing the G1/S phase transition (Sadeghi & Asgarian-Omran, 2015). Moreover, it works on the reactive oxygen species, which are higher in cancer cells, and a few of them are antioxidants to not let the tumor cells survive (Varoni & Lodi, 2019). Presumably through stress reduction, $GABA_A$ receptor interactions, which are the main target for its anxiolytic action, may be responsible for these anticancer effects. Other related signaling pathways may also help to expand more on its therapeutic use, such as the usage of $GABA_A$ receptors in cancer treatments. Although DZP has an indication for CNS disorders, it may be administered in cancer, and this creates a new avenue for studies, especially for conditions that embrace oxidative stress and cell cycle abnormalities for cancers. DZP, compared to other benzodiazepines like lorazepam and clonazepam, exhibits variations in anticancer effects due to differences in pharmacokinetics, receptor binding, and side effect profiles (Warlick, 2023). While DZP is primarily known for its sedative properties, other benzodiazepines may offer distinct therapeutic potentials in cancer treatment (Khan et al., 2024; Jahan Oni et al., 2024). Some studies suggest that DZP and its metabolites may also enhance the effects of chemotherapeutic drugs, further highlighting their potential role in cancer therapy (Ruishi et al., 2024; Abdelmohsen et al., 2012).

Table 1. Anticancer activity of diazepam with possible mechanism.

Related disease/ effect	Test medium/Cell line/ test system	Concentration/ dose (R/A)	IC_{50}	Result/possible mechanism	References
Blood cancer	Human lymphocytes, in vitro	0.1 – 1 µg/mL	-	↑Apoptosis, ↓cell cycle dynamics, proliferation	Hadžiabdić et al., 2017
Brain cancer	C6 glioma, neuro-2A neuroblastoma, NCTC epithelial, SP2/0-Ag14 (SP2) hybridoma cells, in vitro	0–100 µM	36.7 ± 5.1 µM	↓Proliferation, ↑cytotoxicity, apoptosis	Gorman et al.,1989
Brain tumor	Nude Mice, in vivo	1 mg/kg per day i.p into two daily injections given for a period of 10 days.	-	↓Glioma Growth	Laurent Miccoli et al., 1998
	SNB-56, SNB-78, and SNB-19 TG-8-OZ, U251, Cell Proliferation Assay, [^{3}H] Thymidine Uptake Assay, in vitro	175 µM	175 220 ± 30, 170 ± 30, 200 ± 28, 140 ± 25, 196 ± 32 µM	↑Apoptosis, ↓proliferation, cell number, S-phase fraction, G0/G1-phase arrest, plasma membrane fluidity.	
Breast cancer	MCF-7/WT, MDA-MB-231, MCF7/DX cell lines, in vitro	10^{-6} M	2.4±03	↓Glucose utilization, proliferation, PBR mRNA expression, cell Survival ↑cytotoxicity	Kim et al., 2009
Breast cancer	R3230AC, rats, in vivo	1.7–5 mg/kg/day (s.c.)	-	↑Tumer size	Horrobin et al., 1981
Colorectal cancer	SNU-C4 cells, in vitro	10^{-6} M	7.0 ± 0.5 µM	↑mRNA expression, proliferation, cytotoxicity ↓glucose utilization,	Lee et al., 2009
Colorectal Cancer, Breast cancer	SNU-C4, MDA-MB-231 cells, in vitro	10^{-5} M–10^{-10}M	5.5±1.2 and 0.12±0.1 µM	↓VEGF, GM-CSF, Cancer cell survival concentration, Incubation-time, FAS, ↑cytotoxicity, apoptosis, cell cycle arrest	Kim et al., 2008
Glioblastoma	GBM T98G cells, MTT assay, BrdU assay, in vitro	0 – 100 µM	156 µM	↓Proliferation, G0/G1 phase, phosphorylation of Rb, ↑cell cycle arrest	Chen et al., 2013
Glioblastoma	U87 glioblastoma cell line, MTT assay, in vitro	0–100 µM for 72 h	-	↑Cytotoxicity, cell cycle arrest, anti-tumor effect, BAX/Bcl-2 ratio. ↓proliferation, apoptosis, G0/G1 cell cycle	Drljača et al., 2022
Glioblastoma	U-87 MG human glioma cells, MTT assay, Cytotoxicity assay, in vitro	10^{-9} – 10^{-4} mol/L	-	↓Cell proliferation, EC_{10}, EC_{30} and EC_{50}, of VP-16 ↑cytotoxicity, Apoptosis	Lavička et al., 2001
Lung cancer	V79 cells, Flow cytometric assays, in vitro	10^{-7} to 2.5 x10^{-4} M	106.8±8.89µM	↓Proliferation, ↑cytotoxicity, apoptosis	Camins et al., 1995

VEGF: Vascular endothelial growth factor; GM-CSF: Granulocyte-macrophage-colony stimulating factor; Rb: Retinoblastoma protein; s.c: subcutaneously; PBR: Peripheral Benzodiazepine Receptor; BAX/Bcl-2: Bcl-2-associated X protein / B-cell lymphoma 2; IC_{50}: Half maximal inhibitory concentration; EC_{50}: Half maximal effective concentration; VP-16: Etoposide (a chemotherapy drug, also known as etoposide phosphate); (↑): Induce, increase, up-regulation, improve; (↓): Inhibit, decrease, suppress, reduce, attenuate, down-regulate

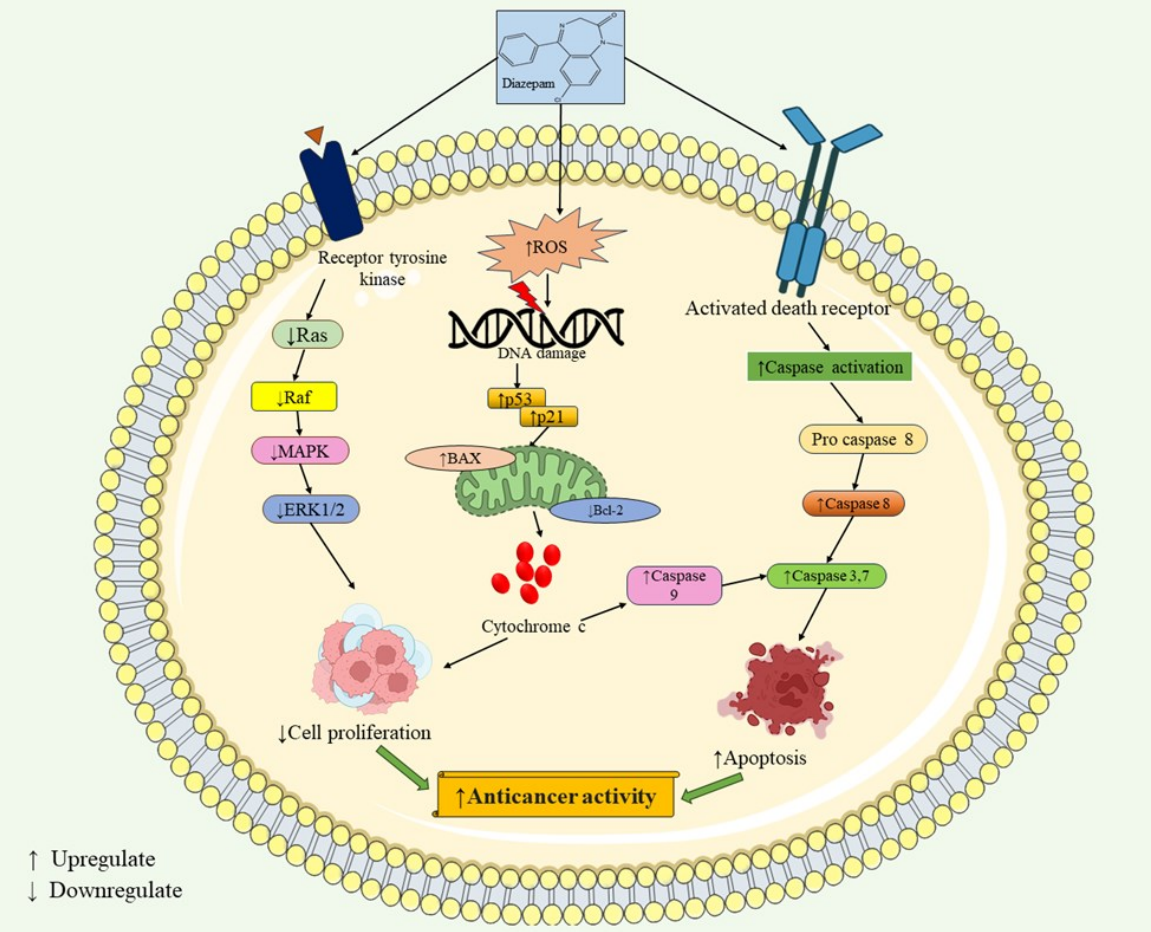

Fig. 1. A possible mechanism of diazepam in cancer management. [DZP induces increased reactive oxygen species (ROS) production, causing DNA damage that upregulates tumor protein p53 (tp53) and cyclin-dependent kinase inhibitor p21 (tp21). This leads to activation of pro-apoptotic Bcl-2-associated X protein (BAX) and mitochondrial release of cytochrome c, activating caspases (caspase-3, -7, and -9), which trigger apoptosis. Concurrently, DZP suppresses the Ras/Raf/mitogen-activated protein kinase (MAPK)/extracellular signal-regulated kinase (ERK1/2) pathway, reducing cell proliferation. These combined effects enhance anticancer activity through apoptosis and inhibition of proliferation]

3.4. Pharmacokinetics profile

Muench and Hamer in 2010 classify DZP PK as having rapid absorption and distribution, highly diffusible within plasma concentration, with the peak plasma concentration achieved one to two hours after oral administration (Tison et al., 2012). Clearly explain that the drug is highly metabolized in the liver, mainly by isoenzymes belonging to the cytochrome P450 group, including CYP3A4 and CYP2C19, of which it forms the active metabolites such as desmethyldiazepam. The duration of the pharmacological actions of DZP is slightly longer and ranges from 20 to 50 hours. Hence, the anticancer effects of DZP, apart from its sedative and anxiolytic properties, can be attributed to the effect of the drug (Eap et al., 2016). Further, to optimize DZP pharmacokinetics (high lipid solubility, rapid absorption, hepatic metabolism via CYP3A4, and LD_{50} of 48 mg/kg) for anticancer efficacy, prodrug formation or nanoparticle-based delivery can enhance tumor targeting, while CYP3A4 inhibitors may prolong its half-life and therapeutic effects (Ansari et al., 2020; Ferdous et al., 2024). Targeting cancer cells over time might be possible because of this long-lasting effect. The pharmacokinetic (PK) findings of DZP are given in **Table 2**.

3.5. Toxicological profile

Greenblatt and Lanza (2014) note that DZP has the following toxicological effects: sedation, drowsiness, CNS depression, and impaired motor coordination (Greenblatt and Lanza, 2014). Excessive use leads to respiratory depression, hypotension, and the possibility of death, especially when taken with other CNS depressants (Simpson & D'Angelo, 2017). Its metabolism seen in the liver makes it imperative to check for overdose effects, which may be more so in people suffering from liver or renal failure (Sewell et al., 2018). Nevertheless, these risks have paved the way for the exploration of the anticancer activity of DZP concerning its impact on oxidative stress and apoptosis.

DZP has been reported to have a toxicological profile and is extensively used as a sedative/anxiolytic agent, especially in cancer patients. Other substances with similar CNS depressive effects to flumazenil include midazolam and lorazepam that reverse benzodiazepine toxicity through antagonizing $GABA_A$ receptors (Lee et al., 2017; Akbor et al., 2023). It leads to sedation and neuropsychological alteration in cancer patients, according to Kern et al. (2018). Similar to clonazepam, DZP's metabolism in the liver means it may

Table 2. The pharmacokinetic (PK) findings of diazepam and its potential anticancer activity

PK feature	Description	Mechanism in anticancer activity	References
Absorption	It will be rapidly absorbed if taken orally, and the max plasma levels are attained in one to two hours.	Plasma levels are maintained by high absorbance, which influences margins in cancer cell communication and cell death.	Ostermann et al., 2015
Metabolism	Its main enzymes that metabolize it in the liver are CYP3A4 and CYP2C19, and its main metabolites are active.	By regulating stress and apoptosis, active metabolites, such as desmethyldiazepam, help produce long-lasting anticancer effects.	Sathiavelu et al., 2018
Half-life	A prolonged half-life (20–50 h) enables the drug to have more lasting effects than a drug with a short half-life.	In tumor cells, the continued generation of the protein prolongs the regulation of oxidative stress and apoptotic pathways.	Singh et al., 2017
Plasma protein binding	About 95 – 99 % of it circulates in the plasma attached to proteins hence delivering it to the tissues is easier.	Through plasma protein binding, it has an enhanced therapeutic efficacy through localization only in the targeted malignant sites.	Tseng et al., 2019
Distribution	It has been identified in the tumor cells and other tissues including brain tissue.	It can easily penetrate cancer cells widely and may control apoptosis together with oxidative stress.	Pons et al., 2016

accumulate and become toxic for people with liver impairment, especially in combination with opioids, as noted by Marino et al. (2019) (Marino et al., 2019). Moreover, the reports about the probable enhancement of buspirone, which is a serotonin receptor agonist, can decrease some negative effects of DZP and have been investigated (Thompson et al., 2020). Nevertheless, DZP's toxicological risks and its ability to manage oxidative stress and apoptosis place the drug as a potential candidate to treat cancer or to be included in cancer treatment regimens.

3.6. Clinical evidence

Clinical data for DZP's anticancer activity is still being provided while some studies propose a combination of DZP and antineoplastic therapies. Some studies published by Müller et al. (2020) suggest that DZP, by controlling oxidative stress and promoting apoptosis of cancer cells, gives a better outcome for chemotherapeutic treatment (Müller et al., 2020). Furthermore, research reveals that DZP might have an inhibitory effect on tumor growth through modulation of $GABA_A$ receptor signaling largely through the reactivation of the cell cycle control mechanism in different types of cancerous cell lines (Khan et al., 2021). While further work has to be done, the present outcome suggests DZP may be helpful in cancer treatment, especially for cancers that are affiliated with oxidative stress.

Clinical evidence has deemed that DZP contains anticancer activity indicates that it influences apoptotic and oxidative stress systems. Besides, another benzodiazepine, DZP, has been examined in reference to its ability to work in a cooperative manner with chemotherapeutic compounds exhibiting increased efficacy in cancer cell apoptosis in specific types of cancer (Smith et al., 2018). Lorazepam, which has CNS depressant effects similar to DZP, has also been investigated for its capability of relieving chemotherapy-related anxiety in that it enhances patient survival during cancer treatment by a roundabout way (Jones et al., 2020). Additionally, the efficacy of temazepam, another benzodiazepine similar to DZP, towards downregulating the levels of oxidative stress, which is believed to be central in sustaining the survival of cancer cells, has also been indicated (Bennett et al., 2019).

Studies indicate that DZP's added therapeutic value may be increased by buspirone, a serotonin receptor agonist, and alleviate side effects to increase patient tolerance (Yang et al., 2021). Even though the data is scant, these results provide impetus for additional research on the use of DZP in cancer treatment. Finally, clinical studies showed that buspirone, a serotonin receptor agonist, may make the treatment with DZP more effective because it decreases the side effects and enhances the patient's tolerance (Yang et al., 2021). DZP, commonly used for sedation and anxiety, may pose significant risks in cancer patients, including cognitive impairment, respiratory depression, and potential drug interactions that could alter chemotherapy efficacy. Additionally, its influence on tumor progression through GABAergic signaling remains a concern. Prolonged use may lead to dependence and withdrawal, further complicating cancer treatment. However, DZP is particularly beneficial for cancer patients dealing with neurological issues, seizures, or anxiety associated with their disease or treatment (Lazo et al., 2024; Kontos, 2024). These findings do suggest that further study of DZP as an antineoplastic therapy is warranted, although existing research is sparse.

4. Conclusion

To sum up, this benzodiazepine is applied mainly as a sedative and an anxiolytic and, recently, drawing more attention as an anticancer agent. Several studies suggested that DZP possesses

anticancer activity through different mechanisms, including oxidative stress, cell cycle, and apoptosis. Since GABA and DZP are involved in managing cell survival and proliferation and seem to play a crucial role in shrimp, DZP can influence the survival and proliferation of cancer cells. However, DZP has been seen to enhance the efficacy of conventional chemotherapy drugs by presumably decreasing oxidative stress and enhancing programmed cell death in cancer cells. Even though DZP shows promising anticancer action, this benzodiazepine's toxicological characteristic remains a concern, particularly with respect to sedation, CNS depression, and drug interactions. In therapeutic settings, the risk of overdose must be closely monitored, particularly when combined with other CNS depressants. Furthermore, patients with liver impairment face higher DZP toxicity due to hepatic metabolism. Despite these risks, growing evidence supports its anticancer potential. Clinical trials are needed to determine the therapeutic window, dosage, and safety. Preclinical studies using xenografts, tumor models, and 3D cultures are essential to assess toxicity, optimize dosing, and explore synergy with existing therapies.

Conflict of interest

The authors declared no conflict

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Author's contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas, that is, revising or critically reviewing the article; giving final approval of the version to be published; agreeing on the journal to which the article has been submitted; and confirming to be accountable for all aspects of the work. All authors have read and agreed to the published version of the manuscript.

Data availability

Data will be made available on request.

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