INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Review Article

A Review on "Apoptosis in Cancer: From Pathogenesis to Cancer''

Ajeet Kumar*[1], Sana Nusrat Praween[2]

[1]*B. Pharmacy VIII- Semester Students, Aryabhatta Knowledge University, A and E College of Pharmacy, Baluahi, Mohiuddin Nagar, Samastipur, Bihar.*
[2]*Assistant Professor, Faculty of Pharmaceutical Sciences, A and E College of Pharmacy, Baluahi, Mohiuddin Nagar, Samastipur, Bihar.*

ARTICLE INFO

Published: 18 Sept. 2025
Keywords:
Apoptosis, Cell proliferation, Tumor suppressor, Tumor microenvironment (TME), Cancer therapy, Cell homeostasis, Cancer resistance, Pro-oncogenic effects, Immune response, Phagocytes, DNA damage, Metastasis
DOI:
10.5281/zenodo.17149896

ABSTRACT

Apoptosis is a natural, regulated process of cell death that maintains tissue health by removing damaged or dangerous cells. It is crucial in both normal body functions and disease conditions. When apoptosis is disrupted, it can lead to diseases—excessive apoptosis is linked to degenerative disorders, while insufficient apoptosis is a major factor in cancer. In cancer, the imbalance between rapid cell growth and reduced cell death allows abnormal cells to survive and spread. Interestingly, some cancers show high levels of apoptosis, which can help suppress tumor growth. However, this process is complex. In some cases, limited apoptosis can influence the tumor microenvironment (TME) in ways that actually support cancer growth and resistance to treatment. The dual nature of apoptosis—both suppressing and potentially supporting tumors—makes it a challenging yet promising target for cancer therapies. Researchers are developing drugs to enhance apoptosis, but these require thorough testing to ensure safety and effectiveness.

INTRODUCTION

1.0 Introduction – Role of Apoptosis in Cancer

Apoptosis is a natural, tightly regulated process of programmed cell death vital for development and tissue maintenance. It acts as a defense mechanism by eliminating damaged or dangerous cells, and can be triggered by factors like infections, DNA damage, and cancer treatments. Central to apoptosis are caspase enzymes, activated through internal (mitochondrial) or external (receptor-mediated) pathways. In cancer, tumor cells often avoid apoptosis, helping them survive, multiply,

***Corresponding Author:** Ajeet Kumar
Address: *B. Pharmacy VIII- Semester Students, Aryabhatta Knowledge University, A and E College of Pharmacy, Baluahi, Mohiuddin Nagar, Samastipur, Bihar.*
Email ✉: ajeetkumar05511@gmail.com
Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

and resist therapy. Some aggressive cancers even show high apoptosis levels, suggesting that dying tumor cells might aid tumor growth under certain conditions. The disruption of the balance between cell division and cell death is a key feature in cancer. For instance, mutations in the tumor-suppressor gene p53, which promotes apoptosis, are common. Additionally, treatments that kill cancer cells may unintentionally promote tumor recovery by altering the surrounding tumor microenvironment (TME). Therefore, effective cancer therapies must not only target tumor cells but also address their complex interactions within the TME to overcome resistance and improve treatment outcomes.[1]

2.0 Morphological Changes in Apoptosis

Apoptosis, or programmed cell death, involves distinct and orderly structural changes in both the nucleus and cytoplasm of the cell. These changes are consistent across various cell types and usually take several hours to complete, depending on the cell type and stimulus.

2.1 Nuclear Changes

- **Chromatin Condensation**: DNA and proteins (chromatin) condense near the nuclear membrane, forming crescent or ring shapes.
- **Nuclear Fragmentation (Karyorrhexis)**: The condensed chromatin breaks apart, while the cell membrane remains intact—unlike necrosis.

2.2 Cytoplasmic and Cellular Changes

- **Cell Shrinkage and Rounding**: The cell becomes smaller and rounder (pyknosis).
- **Retraction of Pseudopodes**: The cell pulls in its projections used for movement.
- **Membrane Blebbing**: The outer membrane forms bubble-like blebs—a key sign of late-stage apoptosis.
- **Ultrastructural Modifications**: Internal organelles change in preparation for controlled breakdown.[2]

Importantly, during apoptosis, the cell's outer membrane stays intact, preventing inflammation and distinguishing it from uncontrolled cell death processes like necrosis.

2.3 Final Stages and Clearance of Apoptosis

In the final phase of apoptosis, the cell breaks into small, membrane-enclosed fragments called **apoptotic bodies**, which safely contain parts of the nucleus and cytoplasm. These are quickly recognized and removed by nearby **phagocytes** (immune cells), ensuring no harmful substances leak out. This rapid and clean removal explains why apoptotic bodies are rarely observed under normal conditions.

2.4 Secondary Necrosis

If apoptotic cells are **not cleared in time**—such as in lab settings without phagocytes—they eventually undergo **secondary necrosis**, where the membrane breaks down. This process resembles necrosis and may lead to **inflammation**, unlike the controlled nature of normal apoptosis.

3.0 Biochemical Changes in Apoptosis

Apoptosis involves a series of organized **biochemical events** that dismantle the cell without causing inflammation. These changes are mainly grouped into **three categories**: caspase activation, DNA/protein breakdown, and membrane alterations aiding phagocytosis.

3.1 Activation of Caspases

Caspases are key enzymes that get activated during apoptosis. They cleave specific proteins and activate DNA-degrading enzymes, leading to controlled disassembly of the cell's structure and function.

3.2 DNA and Protein Breakdown

Apoptotic cells show distinct **DNA fragmentation**. DNA is first broken into large pieces, then into smaller, 180–200 base-pair fragments forming a **DNA ladder**—a hallmark of apoptosis. However, this pattern is not exclusive to apoptosis and may appear in necrosis too.

3.3 Membrane Changes and Recognition by Phagocytes

A key membrane change is the flipping of **phosphatidylserine (PS)** from the inner to the outer membrane, signaling phagocytes to engulf the dying cell. This prevents inflammation and supports clean cell removal.[3]

3.4 Limitations and Considerations

While **biochemical markers** like caspase activity and DNA fragmentation help detect apoptosis, they have limitations. Not all apoptosis follows the same pathways—some may be **caspase-independent**. Hence, experts recommend emphasizing **morphological features** for accurate identification of apoptosis.

4.0 Mechanisms of Apoptosis

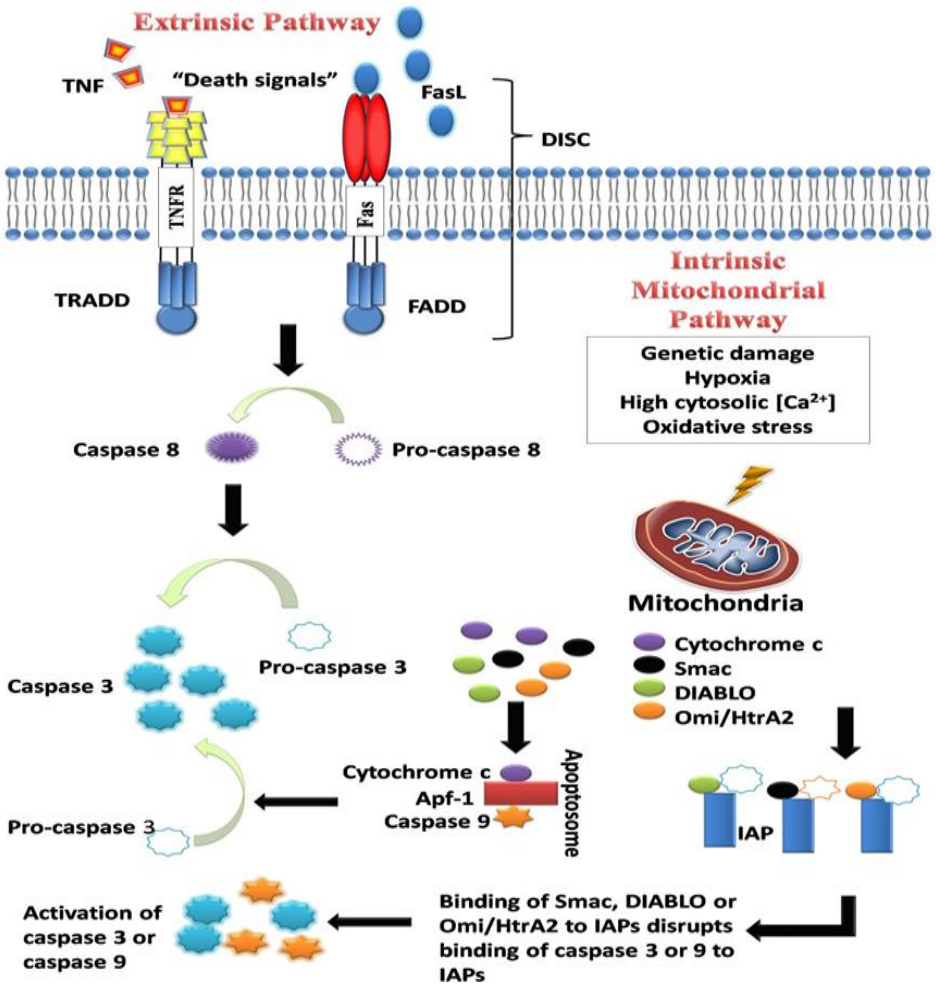

Fig 01:- The intrinsic and extrinsic pathways of apoptosis [12]

Understanding how apoptosis is triggered and regulated is crucial, as disruptions in these mechanisms are linked to many diseases, including cancer. The process is mainly driven by **caspases**, which act as both initiators and executors of cell death. There are **three key pathways** that activate apoptosis:

4.1 Extrinsic (Death Receptor) Pathway

This pathway is triggered by external signals, where death ligands (like TNF or FasL) bind to specific death receptors (TNFR1, Fas/CD95) on the cell surface. This binding forms a complex called DISC (Death-Inducing Signaling Complex), which activates caspase 8, an initiator enzyme. Caspase 8 then activates downstream executioner caspases, leading to controlled cell death.

4.2 Intrinsic (Mitochondrial) Pathway

This pathway starts from within the cell, usually due to internal stress like DNA damage, oxidative stress, or calcium imbalance. These stress signals increase mitochondrial membrane permeability, causing the release of cytochrome c and other apoptotic proteins. Cytochrome c helps form the apoptosome complex, which activates caspase 9. The pathway is tightly regulated by the Bcl-2 protein family, where pro-apoptotic members (e.g., Bax, Bak) promote cell death and anti-apoptotic members (e.g., Bcl-2, Bcl-XL) try to prevent it. Additional proteins like Smac/DIABLO and Omi/HtrA2 enhance apoptosis by blocking caspase inhibitors.[4]

4.3 The Common Execution Pathway

Both the extrinsic and intrinsic apoptotic pathways ultimately activate the common execution phase, centered around caspase 3, the key executioner enzyme. Caspase 9 (intrinsic) and caspase 8 (extrinsic) both activate caspase 3, which then cleaves the inhibitor of caspase-activated DNase (CAD), leading to DNA fragmentation—a hallmark of apoptosis. Caspase 3 also targets various other cellular components, including kinases, cytoskeletal proteins, DNA repair enzymes, and more. These cleavages cause structural and functional breakdowns in the cell, such as membrane blebbing, cytoskeleton collapse, and the formation of apoptotic bodies, ensuring an orderly dismantling process.

4.4 The Intrinsic Endoplasmic Reticulum (ER) Pathway

The ER stress-induced pathway is a third, less common apoptotic route, triggered by cellular stress like hypoxia, oxidative damage, or glucose deprivation, which leads to protein misfolding in the ER. This activates caspase 12, independent of mitochondria.[5]. Activation occurs when TRAF2 dissociates from procaspase 12, initiating a cascade that leads to apoptosis. This ER pathway provides an additional layer of regulation, allowing cells to respond to internal stress not directly involving mitochondria.

5.0 Apoptosis and Carcinogenesis

Apoptosis plays a crucial role in preventing cancer by eliminating damaged or abnormal cells. However, cancerous cells often evade apoptosis, enabling unchecked growth and survival. This evasion is considered a hallmark of cancer and occurs through several mechanisms:

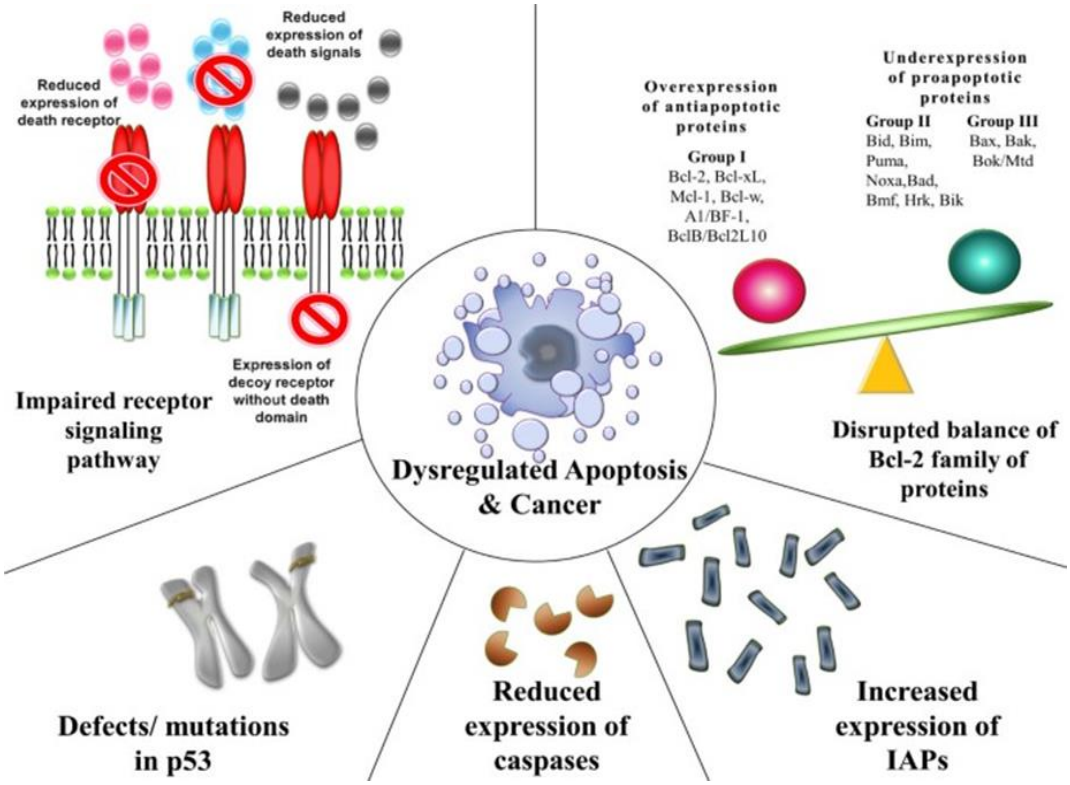

Fig 02:-Mechanisms contributing to evasion of apoptosis and carcinogenesis.[13]

1.Imbalance between pro- and anti-apoptotic protein

2.Reduced caspase activity

3.Defects in death receptor signalling

These changes allow malignant cells to resist death signals, persist, and accumulate further mutations.

5.1.1 Disrupted Balance of Pro-apoptotic and Anti-apoptotic Proteins

A key regulatory group in apoptosis is the Bcl-2 family, which includes both anti-apoptotic and pro-apoptotic members. The relative balance, rather than absolute levels, of these proteins determines a cell's fate.

- **Anti-apoptotic proteins** (e.g., Bcl-2, Bcl-xL, Mcl-1) prevent mitochondrial membrane permeabilization.
- **Pro-apoptotic effector proteins** (e.g., Bax, Bak) promote apoptosis by increasing membrane permeability.
- **BH3-only proteins** (e.g., Bid, Bim, Puma) sense stress and initiate apoptosis.

Cancer cells often overexpress anti-apoptotic proteins (e.g., Bcl-2 in prostate cancer, Bcl-xL in drug-resistant tumors) or downregulate pro-apoptotic ones (e.g., Bax mutations in colorectal cancer), leading to reduced apoptosis and therapy resistance.[6]

5.1.2 p53

p53, known as "the guardian of the genome," is a tumor suppressor protein that regulates the cell cycle and apoptosis in response to DNA damage. The TP53 gene is mutated in over 50% of cancers, impairing apoptosis and enabling tumor progression.

- Mutant p53 can **lose its** protective function or gain oncogenic activity.
- Aberrant p53 is linked to enhanced cell survival, reduced apoptosis, and increased inflammation in cancers like melanoma.
- Targeting mutant p53 in some cancers can restore apoptosis and reduce tumor growth.

5.1.3 Inhibitor of Apoptosis Proteins (IAPs)

IAPs are a family of proteins that block apoptosis by inhibiting caspases directly or promoting their degradation. They contain BIR domains that bind caspases and prevent cell death.

- Overexpression of IAPs in cancer cells helps them resist apoptosis.
- Targeting IAPs is an emerging strategy for sensitizing cancer cells to therapy.

5.2 Reduced Caspase Activity

Caspases are critical enzymes involved in apoptosis and inflammation. In cancer, reduced expression or loss of caspase activity impairs apoptosis, allowing abnormal cells to survive, proliferate, and resist treatment—contributing to carcinogenesis.

Types of Caspases:

- **Inflammation-related caspases**: Caspase-1, -4, -5, -13, -14 (cytokine processing)
- **Apoptosis-related caspases**:
  - **Initiator caspases**: Caspase-2, -8, -9, -10 (trigger apoptosis)
  - **Effector caspases**: Caspase-3, -6, -7 (execute apoptosis)

Clinical Evidence of Caspase Downregulation in Cancer:

- Caspase-9 is frequently downregulated in stage II colorectal cancer, correlating with poor outcomes.
- Caspase-3 is absent or significantly reduced in breast, cervical, and ovarian cancers (e.g., MCF-7 breast cancer cells). Restoring caspase-3 reactivates apoptosis and increases treatment sensitivity.
- Caspase-8 and -10 are simultaneously downregulated in choriocarcinoma, severely disrupting apoptotic signaling.[7]

5.3 Impaired Death Receptor Signaling

The extrinsic pathway of apoptosis is initiated by death receptors located on the cell surface, which respond to external death signals (ligands) like FasL, TNF, and TRAIL. These receptors include TNFR1, Fas (CD95), DR3, DR4, DR5, and others, each containing a death domain that activates downstream caspases to induce apoptosis.

Mechanism of Normal Death Receptor Function:

- Binding of death ligands triggers the formation of Death-Inducing Signalling Complex (DISC).
- This activates initiator caspases, leading to cell death.

Mechanisms of Impairment in Cancer:

1. **Downregulation or Loss of Receptor Expression:**
   - Lower levels of receptors like **CD95** reduce apoptosis sensitivity.

- Found in treatment-resistant **leukemia and neuroblastoma**.

2. **Overexpression of Decoy Receptors:**

- Decoy receptors mimic real receptors but **lack death domains**, blocking the apoptotic signal.

3. **Mutations or Defects in Death Receptors:**

- Even if receptors are present, **mutations in their structure** can prevent DISC formation and signal transmission.

4. **Reduced Death Ligands:**

- Decreased availability of **FasL or TRAIL** weakens the extrinsic apoptotic pathway.[8]

6.0 Targeting the Bcl-2 Family in Cancer Therapy

1. Antisense Inhibitors

- **Oblimersen sodium (G3139)**: A synthetic antisense oligonucleotide that binds to Bcl-2 mRNA, preventing its translation and leading to decreased Bcl-2 protein levels.
- **Effect**: Sensitizes cancer cells to chemotherapy by promoting apoptosis.

2. Small Molecule Inhibitors

- **Examples**: Gossypol, TW-37, ABT-737, ABT-263 (Navitoclax)
- **Mechanism**: These compounds directly bind and inhibit anti-apoptotic Bcl-2 family proteins, allowing pro-apoptotic proteins to initiate cell death.

3. BH3 Mimetics

- **Function**: Imitate BH3-only proteins, displacing pro-apoptotic proteins from Bcl-2 complexes.
- **Result**: Facilitates mitochondrial outer membrane permeabilization (MOMP), leading to apoptosis.

4. Gene Silencing

- **Approach**: Use of small interfering RNAs (siRNAs) to knock down expression of Bcl-2 and related genes (e.g., Bmi-1).

Impact: Increases cancer cell susceptibility to apoptosis and reduces therapy resistance.

6.1Targeting Apoptosis in Cancer Therapy

Apoptotic pathways, when disrupted, not only contribute to cancer development but also offer promising targets for treatment. Defects or abnormalities within these pathways can be exploited therapeutically—by designing drugs or interventions that restore normal apoptotic signaling, it becomes possible to selectively eliminate cancer cells that rely on such defects for survival. Recent advances in research have led to the discovery of novel anticancer agents that specifically target these apoptotic dysfunctions[14]. This section focuses on emerging treatment strategies aimed at correcting the apoptotic defects discussed earlier in Section 3. For a detailed overview of these drugs and approaches, please refer to Table 1.

Targeting the Bcl-2 family of proteins	Remark

Agents that target the Bcl-2 family proteins	*Oblimersen sodium*
	Reported to show chemosensitising effects in combined treatment with conventional anticancer drugs in chronic myeloid leukaemia patients and an improvement in survival in these patients
	Small molecule inhibitors of the Bcl-2 family of proteins
	Molecules reported to affect gene or protein expression include sodium butyrate, depsipetide, fenretinide and flavipirodo. Molecules reported to act on the proteins themselves include gossypol, ABT-737, ABT-263, GX15-070 and HA14-1
	BH3 mimetics
	ABT-737 reported to inhibit anti-apoptotic proteins such as Bcl-2, Bcl-xL, and Bcl-W and to exhibit cytotoxicity in lymphoma, small cell lung carcinoma cell line and primary patient-derived cells
	ATF4, ATF3 and NOXA reported to bind to and inhibit Mcl-1
Silencing the Bcl family anti-apoptotic proteins/genes	Bcl-2 specific siRNA reported to specifically inhibit the expression of target gene *in vitro* and *in vivo* with anti-proliferative and pro-apoptotic effects observed in pancreatic carcinoma cells
	Silencing Bmi-1 in MCF breast cancer cells reported to downregulate the expression of pAkt and Bcl-2 and to increase sensitivity of these cells to doxorubicin with an increase in apoptotic cells *in vitro* and *in vivo*
Targeting p53	
p53-based gene therapy	First report on the use of a wild-type p53 gene containing retroviral vector injected into tumour cells of non-small cell lung carcinoma derived from patients. The use of p53-based gene therapy was reported to be feasible.
	Introduction of wild type p53 gene reported to sensitise tumour cells of head and neck, colorectal and prostate cancers and glioma to ionising radiation
	Genetically engineered oncolytic adenovirus, ONYX-015 reported to selectively replicate in and lyse tumour cells deficient in p53
p53-based drug therapy	*Small molecules*
	Phikan083 reported to bind to and restore mutant p53
	CP-31398 reported to intercalate with DNA and alter and destabilise the DNA-p53 core domain complex, resulting in the restoration of unstable p53 mutants

	Other agents
	Nutlins reported to inhibit the MSM2-p53 interaction, stabilise p53 and selectively induce senescence in cancer cells
	MI-219 reported to disrupt the MDM2-p53 interaction, resulting in inhibition of cell proliferation, selective apoptosis in tumour cells and complete tumour growth inhibition
	Tenovins reported to decrease tumour growth *in vivo*
p53-based immunotherapy	Patients with advanced stage cancer given vaccine containing a recombinant replication-defective adenoviral vector with human wild-type p53 reported to have stable disease
	Clinical and p53-specific T cell responses observed in patients given p53 peptide pulsed dendritic cells in a phase I clinical trial
Targeting IAPS	
Targeting XIAP	*Antisense approach*
	Reported to result in an improved *in vivo* tumour control by radiotherapy
	Concurrent use of antisense oligonucleotides and chemotherapy reported to exhibit enhanced chemotherapeutic activity in lung cancer cells *in vitro* and *in vivo*
	siRNA approach
	siRNA targeting of XIAP reported to increase radiation sensitivity of human cancer cells independent of TP53 status
	Targeting XIAP or Survivin by siRNAs sensitised hepatoma cells to death receptor- and chemotherapeutic agent-induced cell death
Targeting Survivin	*Antisense approach*
	Transfection of anti-sense Survivin into YUSAC-2 and LOX malignant melanoma cells reported to result in spontaneous apoptosis
	Reported to induce apoptosis and sensitise head and neck squamous cell carcinoma cells to chemotherapy
	Reported to inhibit growth and proliferation of medullary thyroid carcinoma cells
	siRNA approach
	Reported o downregulate Survivin and diminish radioresistance in pancreatic cancer cells

	Reported to inhibit proliferation and induce apoptosis in SPCA1 and SH77 human lung adenocarcinoma cells
	Reported to suppress Survivin expression, inhibit cell proliferation and enhance apoptosis in SKOV3/DDP ovarian cancer cells
	Reported to enhance the radiosensitivity of human non-small cell lung cancer cells
Other IAP antagonists	*Small molecules antagonists*
	Cyclin-dependent kinase inhibitors and Hsp90 inhibitors and gene therapy attempted in targeting Survivin in cancer therapy
	Cyclopeptidic Smac mimetics 2 and 3 report to bind to XIAP and cIAP-1/2 and restore the activities of caspases- 9 and 3/-7 inhibited by XIAP
	SM-164 reported to enhance TRAIL activity by concurrently targeting XIAP and cIAP1
Targeting caspases	
Caspase-based drug therapy	Apoptin reported to selectively induce apoptosis in malignant but not normal cells
	Small molecules caspase activators reported to lower the activation threshold of caspase or activate caspase, contributing to an increased drug sensitivity of cancer cells
Caspase-based gene therapy	Human caspase-3 gene therapy used in addition to etoposide treatment in an AH130 liver tumour model reported to induce extensive apoptosis and reduce tumour volume
	Gene transfer of constitutively active caspse-3 into HuH7 human hepatoma cells reported to selectively induce apoptosis
	A recombinant adenovirus carrying immunocaspase 3 reported to exert anticancer effect in hepatocellular carcinoma *in vitro* and *in vivo*

6.2 Targeting p53

6.2.1 p53-Based Gene Therapy

- **Strategy**: Use of viral vectors to deliver wild-type p53 into tumor cells.
- **Key Example**: ONYX-015, an engineered adenovirus that selectively replicates in p53-deficient cancer cells.
- **Results**: Combined gene therapy with treatments like radiation increased tumor sensitivity; some approaches reached phase III trials, but none received FDA approval.

6.2.2 p53-Based Drug Therapy

- **Small Molecules**:

- **Phikan083 & CP-31398**: Restore function to mutant p53 proteins.
- **Nutlins & MI-219**: Inhibit MDM2-p53 interaction, stabilizing and reactivating p53.
- **Tenovins**: Activate p53, reducing tumor growth in animal models.

6.2.3 p53-Based Immunotherapy

- **Vaccines**: Use adenoviral vectors containing wild-type p53 to trigger immune response; some patients showed disease stabilization.
- **Dendritic Cell Therapy**: Dendritic cells pulsed with p53 peptides activated T-cells and showed clinical responses in early trials.
- **Peptide-Based Vaccines**: Trials ongoing to further stimulate immunity against tumor cells with abnormal p53.[9]

6.3 Introduction to IAPs

Inhibitor of Apoptosis Proteins (IAPs) are a family of proteins that prevent cell death by blocking caspases, which are essential for the execution of apoptosis. Their overexpression in cancer cells contributes to therapy resistance and tumor survival, making them a key target in cancer therapy.

6.3.1 XIAP Targeting Approaches

XIAP (X-linked inhibitor of apoptosis protein) is the most potent caspase inhibitor in the IAP family, directly blocking caspase-9, -3, and -7. Therapeutic strategies such as antisense oligonucleotides and siRNAs have been developed to silence XIAP expression. These approaches enhance the effectiveness of radiation and chemotherapy in various cancers, including liver and p53-deficient tumors, by sensitizing the cells to undergo apoptosis.

6.3.2 Targeting Survivin

Survivin is another major IAP family member, widely overexpressed in many types of cancer. It supports tumor cell survival and therapy resistance. Antisense oligonucleotides targeting Survivin induce apoptosis in cancers like melanoma, head and neck, and thyroid. Similarly, siRNA-mediated inhibition of Survivin sensitizes pancreatic, lung, ovarian, and other cancers to radiotherapy and chemotherapy. Small-molecule inhibitors such as CDK inhibitors and Hsp90 inhibitors also suppress Survivin function, promoting cancer cell death.[10]

6.3.4 Use of Smac/DIABLO Mimetics

Smac/DIABLO mimetics are designed to imitate natural IAP inhibitors and restore caspase activity. These compounds target XIAP and other IAPs like cIAP1 to promote apoptosis. Examples include Smac mimetics “2” and “3,” and a non-peptidic Smac mimetic called SM-164. SM-164 inhibits both XIAP and cIAP1, enhancing TRAIL-induced apoptosis in cancer cells. These agents hold great promise in restoring the apoptotic capacity of cancer cells and improving treatment outcomes.

6.4 Targeting Caspases

Caspases, essential enzymes that execute apoptosis, are being actively explored as therapeutic targets in cancer treatment. Two main strategies—drug therapy and gene therapy—aim to restore caspase activity and promote cancer cell death. In caspase-based drug therapy, agents like Apoptin have shown the ability to induce apoptosis specifically in cancer cells without harming normal ones. Additionally, small molecules containing the RGD motif can directly

activate procaspase-3, enhancing the apoptotic response and improving the efficacy of chemotherapy. Gene therapy approaches involve delivering caspase genes directly into tumors. For instance, introducing the caspase-3 gene in combination with chemotherapy in liver tumor models led to greater tumor reduction than chemotherapy alone. Similarly, using constitutively active caspase-3 in liver cancer cells or employing recombinant adenoviruses carrying immunocaspase-3 has proven effective in inducing targeted apoptosis in cancer cells, both in vitro and in vivo.

6.5 Molecules Targeting Apoptosis in Clinical Trials

Numerous apoptosis-modulating compounds have entered clinical trials, as documented in global registries like ClinicalTrials.gov. These investigational agents primarily target crucial apoptotic regulators, including members of the Bcl-2 family and IAPs. Their ongoing clinical evaluation reflects growing interest in leveraging apoptosis restoration as a viable cancer treatment strategy[11].

7.0 CONCLUSION

Research has shown that abnormalities in apoptotic pathways are crucial contributors to cancer development. Promisingly, new therapies that aim to restore or manipulate apoptosis are emerging, offering hope for more effective cancer treatments. Some of these therapies are in early experimental stages, while others have progressed to clinical trials, often being tested alongside traditional cancer drugs to enhance their effectiveness. Despite these advances, several concerns remain unresolved. There is uncertainty about whether tumors might develop resistance to apoptosis-targeting treatments, and whether these therapies might harm healthy cells. These concerns are significant given the known side effects and resistance issues associated with conventional chemotherapy, which tends to affect both cancerous and normal cells indiscriminately. Although the ideal treatment would selectively target a single apoptotic protein or pathway to reduce damage to healthy tissue, most current drugs—such as Bcl-2 inhibitors and IAP antagonists—affect multiple targets. This complexity underscores the need for long-term follow-up studies to assess the true outcomes for patients. Future research should focus on developing treatments that specifically induce apoptosis in cancer cells while sparing normal cells, thereby increasing the effectiveness of therapy and reducing side effects.

REFERENCES

1. Wong, R. S. Y. (2011). Apoptosis in cancer: from pathogenesis to treatment. Cell Death & Disease, 2(12), e249. https://doi.org/10.1038/cddis.2011.142
2. Elmore, S. (2007). Apoptosis: a review of programmed cell death. Toxicologic Pathology, 35(4), 495-516. https://doi.org/10.1080/01926230701320337
3. Johnstone, R. W., Ruefli, A. A., & Lowe, S. W. (2002). Apoptosis: a link between cancer genetics and chemotherapy. Cell, 108(2), 153-164. https://doi.org/10.1016/S0092-8674(02)00625-6
4. Chaudhry, G. S., et al. (2022). Cancer and apoptosis: The apoptotic activity of plant and marine-derived natural products and their potential in cancer therapeutics. Frontiers in Pharmacology, 13, 842376. https://doi.org/10.3389/fphar.2022.842376
5. Cossu, I., et al. (2016). Apoptosis as anticancer mechanism: function and dysfunction of its modulators and targeted therapeutic strategies.

Aging (Albany NY), 8(7), 1448–1475. https://doi.org/10.18632/aging.100934

6. Peng, F., et al. (2022). Regulated cell death (RCD) in cancer: key pathways and therapeutic strategies. Signal Transduction and Targeted Therapy, 7(1), 196. https://doi.org/10.1038/s41392-022-01110-y
7. Moyer, A. (2025). Apoptosis in cancer biology and therapy. Annual Review of Pathology: Mechanisms of Disease, 20, 1-31. https://doi.org/10.1146/annurev-pathmechdis-051222-115023
8. Jänicke, R. U. (2009). Caspase-3: The executioner of apoptosis. Biochemical and Biophysical Research Communications, 329(3), 783-785. https://doi.org/10.1016/j.bbrc.2005.02.085
9. Fulda, S., & Vucic, D. (2012). Targeting IAP proteins for therapeutic intervention in cancer. Nature Reviews Drug Discovery, 11(2), 109–124. https://doi.org/10.1038/nrd3627
10. Vogelstein, B., Lane, D., & Levine, A. J. (2000). Surfing the p53 network. Nature, 408(6810), 307-310. https://doi.org/10.1038/35042675
11. Fulda, S. (2020). Targeting apoptosis for anticancer therapy. Seminars in Cancer Biology, 31(2), 84-96. https://doi.org/10.1016/j.semcancer.2020.03.006
12. Hanahan D, Weinberg RA: The hallmarks of cancer. Cell. 2000, 100: 57-70. 10.1016/S0092-8674(00)81683-9. Article CAS PubMed Google Scholar
13. Vucic D, Stennicke HR, Pisabarro MT, Salvesen GS, Dixit VM: MLIAP, a novel inhibitor of apoptosis that is preferentially expressed in human melanomas. Curr Biol. 2000, 10: 1359-1366. 10.1016/S0960-9822(00)00781-8. Article CAS PubMed Google Scholar.
14. Svane IM, Pedersen AE, Johnsen HE, Nielsen D, Kamby C, Gaarsdal E, Nikolajsen K, Buus S, Claesson MH: Vaccination with p53-peptide-pulsed dendritic cells, of patients with advanced breast cancer: report from a phase I study. Cancer Immunol Immunother. 2004, 53 (7): 633-641. 10.1007/s00262-003-0493-5. Article CAS PubMed Google Scholar.

HOW TO CITE: Ajeet Kumar*, Sana Nusrat Praween, A Review on ‘’Apoptosis in Cancer: From Pathogenesis to Cancer’’, Int. J. of Pharm. Sci., 2025, Vol 3, Issue 9, 1953-1965 https://doi.org/10.5281/zenodo.17149896