Chapter-1

Ayurveda Inspired Discovery of Oral Anti-Cancer Drugs

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Abstract

This review discusses the vast knowledge of natural products with strong emphasis on Ayurveda linked active ingredients for the treatment and management of cancer. RENOVEL uses an approach to integrate these resources and create a new class of orally active drugs for cancer research. Over the last decade, our lab has provided significant stimuli towards developing new class of drugs for major health conditions with multiple ongoing clinical trials. In this review we are extending our core technology towards discovery and development of Ayurveda-based new lead molecules for cancer treatment and management.

Significant progress on cancer research has evolved over the last 50 years. Initial studies discovered altered pathways in normal cell division leading to cancer and developed specific drugs for each targeted pathway. Further research has unfolded increasingly more complex layers of regulation of cancer

cells by the tissue microenvironment, the extracellular matrix, and the surrounding stroma including fibroblasts and immune cells and the gut microbiome. Mental stress, environmental factors, and genetics also have a major role in the development of cancer. Ayurvedic principles outline even more complex levels of regulation on how the cells and tissues interact with and are influenced by the mind, body and environmental factors. Documented clinical trials for cancer treatment with drugs of Ayurvedic origin are limited. The US National Institutes of Health site, Clinical Trials.gov, lists 50 clinical trials (2000–2023) for "Ayurveda" for multiple disease conditions but only a few are for cancer. These trials are mostly conducted in India, Germany, UK, and a few in the USA.

Many Ayurvedic active ingredients have been implicated for ameliorating cancer. It is widely acknowledged that these herbal ingredients deliver bodily homeostasis and suppress the proliferation of tumors. Taking these in consideration along with SAR and bioinformatics, RENOVEL Innovation has synthesized over 40 new Ayurveda-based anti-cancer molecules which are currently in preclinical development. These molecules were screened in 15 human cancer cell lines spanning over 5 major cancer types. In this review, a full overview of growing concern in rapid increase in global cancer with existing drugs, biologics and customized products are discussed along with Ayurveda inspired anti-cancer lead molecule development by RENOVEL.

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1. INTRODUCTION

Cancer is a disease in which the body's cells grow abnormally in an unmanageable manner. The cell growth is accompanied by a rapid formation of abnormal cells along with immature blood vessels. Benign cancers do not spread and are observed within an organ. Cancers can spread to adjoining organs and tissues, a process known as metastasis. [1]

Being a multifactorial disease, the cause and progress of cancer is influenced by a combination of genetic, environmental, and lifestyle factors. Poor diet, inadequate fruit and vegetable intake, tobacco use, alcohol consumption, high body mass index, lack of physical activity, exposure to carcinogens and infections like human papillomavirus (HPV) and hepatitis contribute to the cause and progress of cancer.

Cancer affects nearly 20 million people worldwide each year. The mortality rate from cancer is also high with nearly 10 million deaths per year.

The most common cancers are breast, lung, colon and rectum and prostate cancers. The global cancer incidence presented in

Figure 1 represents almost 50% cases in Asia followed by North America and Europe.[2]

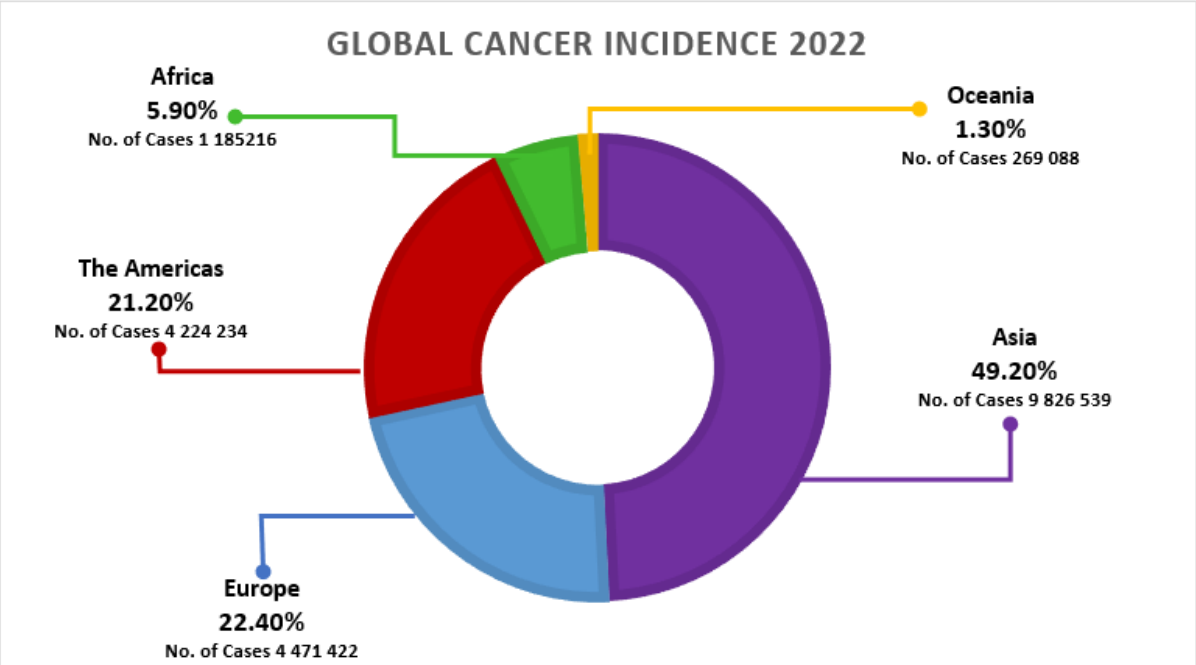


Figure 1: Global Cancer Incidence [3] *(Source: WHO, 2022)*

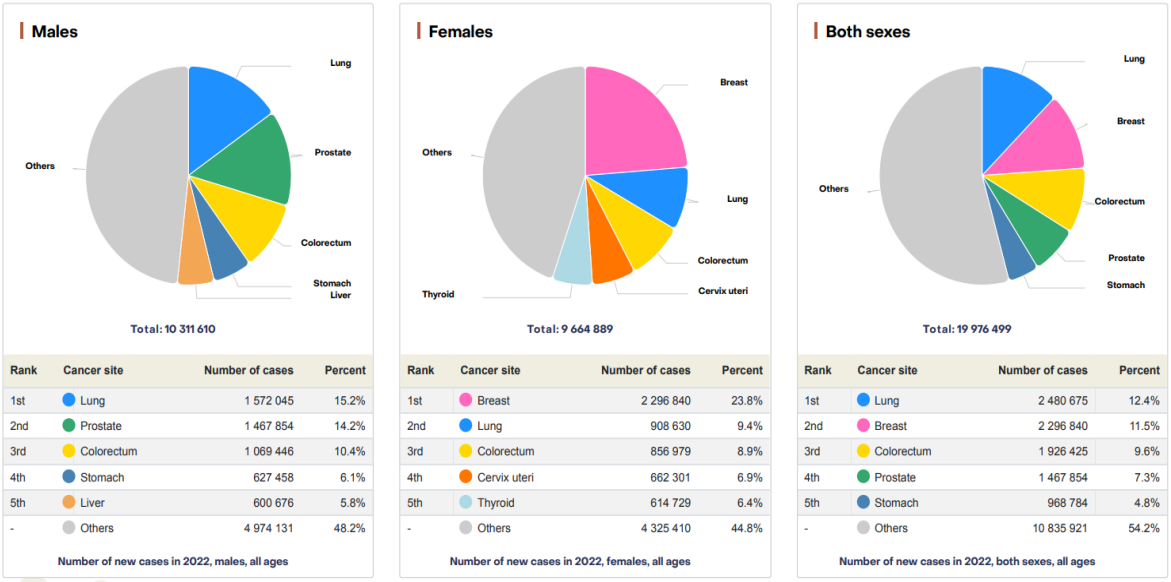
Many new drugs for cancer treatment were discovered from biological markers and natural sources over the last five decades. Natural product-based drug discovery for cancer involves the identification, isolation, and characterization of bioactive compounds from natural sources like plants, marine organisms, fungi, and bacteria. These compounds often possess diverse chemical structures and biological activities that make them attractive candidates for anti-cancer drug development. Understanding the molecular mechanisms underlying the anticancer activity of natural compounds is crucial for the development of drug candidates. Various techniques such as gene expression analysis, proteomics, and molecular modeling are used to discover new class of anti-cancer drugs from natural sources.

Combining untapped ancient knowledge of Ayurvedic medicinal plants with current knowledge of drug discovery science, RENOVEL Innovations is in forefront in identifying new class of natural product-based lead molecules for the treatment and management of major cancer incidences. The company is

focusing on five major cancer types such as breast, prostate, lung, colorectum, and skin which represents nearly 50% of the cancer cases worldwide (

Figure 2).

Structure-Activity-Relationship (SAR) of various pharmacophores in combination with smart chemistry, RENOVEL has synthesized over 40 potential anti-cancer oral molecules that are currently being investigated in cell-based assays and pre-clinical animal models.



Rank	Cancer site	Number of cases	Percent
1st	Lung	1 572 045	15.2%
2nd	Prostate	1 467 854	14.2%
3rd	Colorectum	1 069 446	10.4%
4th	Stomach	627 458	6.1%
5th	Liver	600 676	5.8%
-	Others	4 974 131	48.2%

Number of new cases in 2022, males, all ages

Rank	Cancer site	Number of cases	Percent
1st	Breast	2 296 840	23.8%
2nd	Lung	908 630	9.4%
3rd	Colorectum	856 979	8.9%
4th	Cervix uteri	662 301	6.9%
5th	Thyroid	614 729	6.4%
-	Others	4 325 410	44.8%

Number of new cases in 2022, females, all ages

Rank	Cancer site	Number of cases	Percent
1st	Lung	2 480 675	12.4%
2nd	Breast	2 296 840	11.5%
3rd	Colorectum	1 926 425	9.6%
4th	Prostate	1 467 854	7.3%
5th	Stomach	968 784	4.8%
-	Others	10 835 921	54.2%

Number of new cases in 2022, both sexes, all ages

Figure 2: Five Most Common Cancers Worldwide [4] *(Source: WHO, 2022)*

2. ANTI-CANCER DRUGS FROM NATURAL SOURCES

Several natural products have been implemented for the treatment and management of cancer in recent years. Several ingredients are being investigated by various laboratories globally.

Curcumin is a polyphenolic compound found in turmeric. Curcumin has been used for its anti-inflammatory, antioxidant, and anticancer properties by modulating multiple signaling pathways involved in cancer development and progression. Several clinical trials are undergoing to establish the role of curcumin as a potential anti-cancer natural product. Artemisinin and its derivatives have shown promising anticancer activity by inducing apoptosis in cancer cells and inhibiting tumor growth. Artemisinin is being actively studied for its mechanism of action and potential applications in various cancer types. Taxanes such as paclitaxel and docetaxel are potent anticancer drugs derived from the bark of the Pacific yew tree (*Taxus brevifolia*) and the European yew

tree (*Taxus baccata*), respectively. These compounds interfere with microtubule function, leading to cell cycle arrest and apoptosis in cancer cells. Taxanes are widely used in the treatment of breast cancer, ovarian cancer, and other solid tumors. Vinca alkaloids, including vincristine and vinblastine, are natural compounds extracted from the Madagascar periwinkle plant (*Catharanthus roseus*). These agents disrupt microtubule formation, leading to mitotic arrest and apoptosis in cancer cells. Vinca alkaloids are used in the treatment of leukemia, lymphoma, and various solid tumors. Camptothecin is a plant alkaloid originally isolated from the Chinese tree *Camptotheca acuminata*. Several analogs of camptothecin, such as irinotecan and topotecan, have been developed and approved for the treatment of colorectal cancer, ovarian cancer, and small cell lung cancer. These agents inhibit topoisomerase I, an enzyme involved in DNA replication, leading to DNA damage and cell death.

These are just a few examples, and ongoing research continues to explore the vast potential of natural products in cancer therapy. It's important to note that while natural products offer exciting avenues for drug discovery, rigorous preclinical and clinical studies are necessary to validate their efficacy and safety before widespread clinical use.

3. ROLE OF AYURVEDIC INGREDIENTS IN CANCER MANAGEMENT

Ayurveda, the ancient Indian system of medicine, offers various herbs and ingredients that are believed to have potential benefits in managing cancer.[5,6] Ayurvedic ingredients that have been traditionally used for cancer management include:

- Turmeric (*Curcuma longa*) contains curcumin which has been studied for its potential anti-cancer effects.
- Ashwagandha (*Withania somnifera*) supports the body's ability to cope with stress and has shown some promise in preliminary studies for its anticancer properties.
- Ginger (*Zingiber officinale*) contains gingerol, a bioactive compound that has demonstrated anti-inflammatory and antioxidant effects, which may be beneficial in cancer management.
- Tulsi (*Ocimum sanctum*) also known as holy basil is revered in Ayurveda for its medicinal properties. Some studies suggest that tulsi may have anticancer effects due to its antioxidant and immune-modulating properties.
- Neem (*Azadirachta indica*) is valued in Ayurveda for its various therapeutic properties. Some research indicates that neem extracts may

possess anticancer activity by inducing apoptosis (cell death) in cancer cells.

- Triphala is a combination of three fruits - Amla (*Emblica officinalis*), Haritaki (*Terminalia chebula*), and Bibhitaki (*Terminalia bellirica*). Triphala is commonly used in Ayurvedic medicine for its cleansing and rejuvenating effects. Some studies suggest that it may have potential anticancer properties.
- Guduchi (*Tinospora cordifolia*) also known as Giloy is considered an immunomodulatory herb in Ayurveda and has been studied for its potential anticancer effects.
- Boswellia (*Boswellia serrata*) resin contains boswellic acids, which have demonstrated anti-inflammatory and anticancer properties in some studies.
- Amla (*Emblica officinalis*) rich in vitamin C and antioxidants is believed to have immune-boosting and anticancer properties in Ayurveda.
- Shatavari (*Asparagus racemosus*) is traditionally used in Ayurveda for its rejuvenating and adaptogenic properties. Some studies suggest it may have anticancer effects, particularly in breast cancer.

Table 1 summarizes various herbs from ayurvedic library for the management of various cancers.

Table 1: Ayurvedic Herbs Indicated for Cancer Treatment & Management[7]

S. No.	Common Name	Botanical Name	Family	Part Used
1	Arjuna Bark	Terminalia arjuna	Combertacae	Bark
2	Kalmegh	Andrographis paniculata	Acanthacae	Dried leaves
3	Vinca	Catharanthus roseus	Apocynacae	Whole Plant
4	Ochrosia	Ochrosia elliptica	Apocynacae	Trunk Bark
5	May Apple	Podophyllum peltatum	Berberidacae	Dried Rhizome
6	Ginger	Zingiber officinalis	Zingibaracae	Rhizome
7	Turmeric	Curcuma longa	Zingibaracae	Rhizome
8	Deerberry	Vaccinium stamineum	Ericaceae	Fruit
9	Indian Mulberry	Morinda citrifolia	Rubiaceae	Fruit
10	Bhilwa	Semecarpus anacardium	Anacardiaceae	Fruit
11	Madar	Calotrophis gigantea	Ascelpiadaceae	Whole Plant
12	Arhar Dal	Cajanus cajan	Fabaceae	Leaves
13	Palash	Butea monosperma	Fabaceae	Bark
14	Orchid Tree	Bauhinia variegata	Caesalpinaceae	Root
15	Onion	Alium cepa	Liliaceae	Bulb
16	Indian Aloe	Aloe barbadensis	Liliaceae	Leaves
17	Tarwar	Cassia auriculata	Caesalpinaceae	Root
18	Senna	Cassia senna	Caesalpinaceae	Leaves
19	Lemon	Cassia medica	Rutaceae	Root
20	Carrot	Daucus carota	Apiaceae	Root
21	Danti	Jatropha curcas	Euphorbiaceae	Leaves, seed, oils
22	Mint	Mimosa pudica	Mimosaceae	Whole Plant
23	Ashwagandha	Withania somnifera	Solanaceae	Root
24	Guduchi	Tinospora cordifolia	Menispermacea	Stem
25	Garlic	Allium Sativum	Amaryllidaceae	Bulb
26	Amla	Phyllanthus emblica	Phyllanthaceae	Fruit

While these Ayurvedic ingredients are widely used and have shown promise in some studies, more scientific data and clinical trials are required to establish the role of these Ayurvedic herbs and ingredients in treatment and management of cancer. Phytochemicals from these herbs have potential in combination with other active pharmacophore to develop new class of orally active anti-cancer lead molecules with improved safety profile. Here are few examples of such phytochemicals from amla and turmeric (Figure 3 and Figure 4).

Examples of Bioactive compounds characterized from Amla.

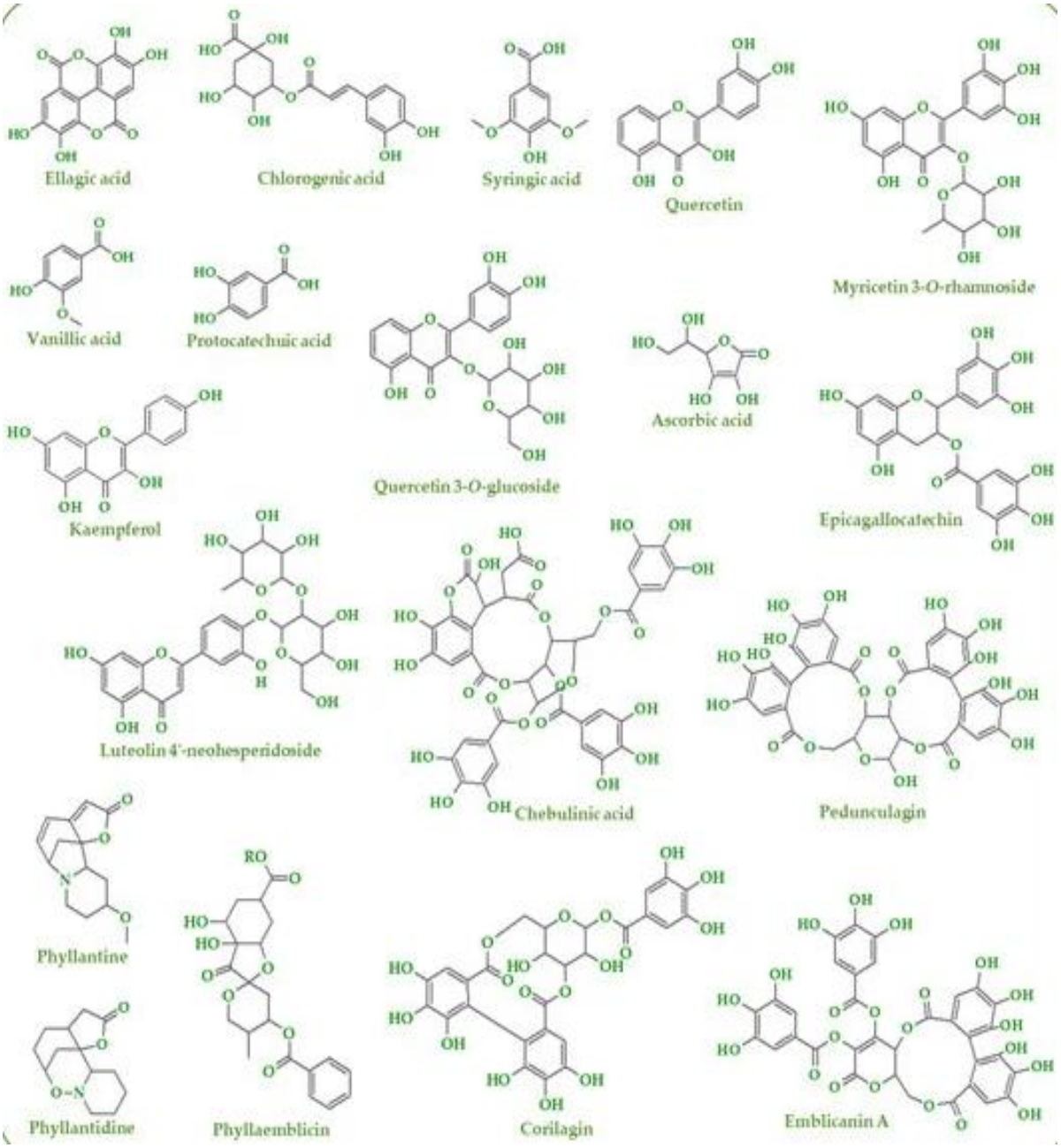


Figure 3: Bioactive compounds from *Embalica Officialis* (Amla) [8]

Examples of Bioactive Compounds from Turmeric

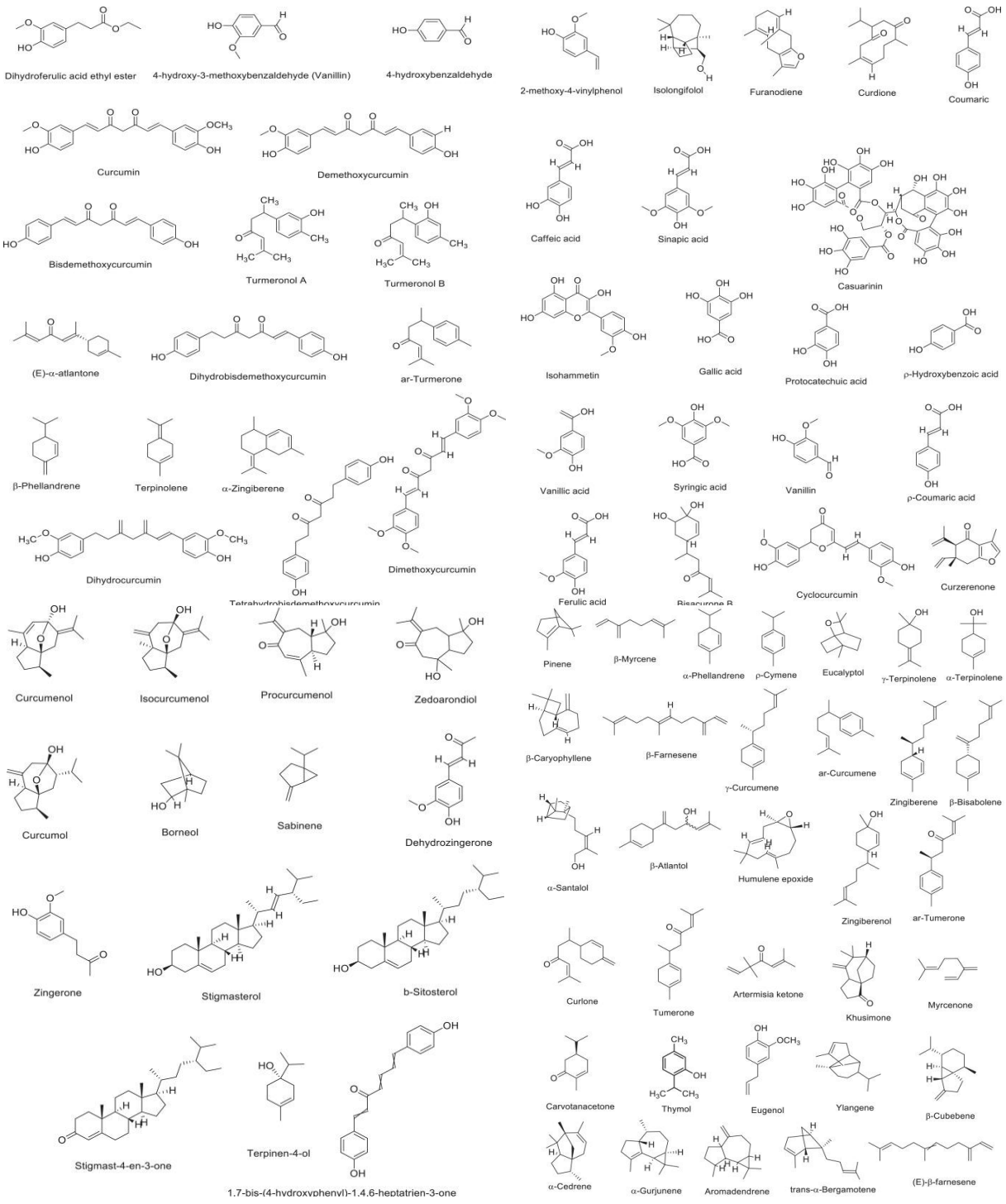


Figure 4: Bioactive compounds and oils from *Curcuma longa* (Turmeric)

4. GENETIC ROLE IN CANCER

Genetics plays an important role in development of various types of cancers. Many studies have already linked genetic involvement in developing cancer. The role of genetics in cancer development is significant, although it's just one aspect of a complex interplay of factors that contribute to the rise of cancer incidence.

Inherited Genetic Mutations: Some individuals inherit genetic mutations from their parents that increase their risk of developing certain types of cancer. These mutations can predispose individuals to cancer by interfering with normal cell growth and repair mechanisms.

Figure **5** represents various cancers with inherited mutations.

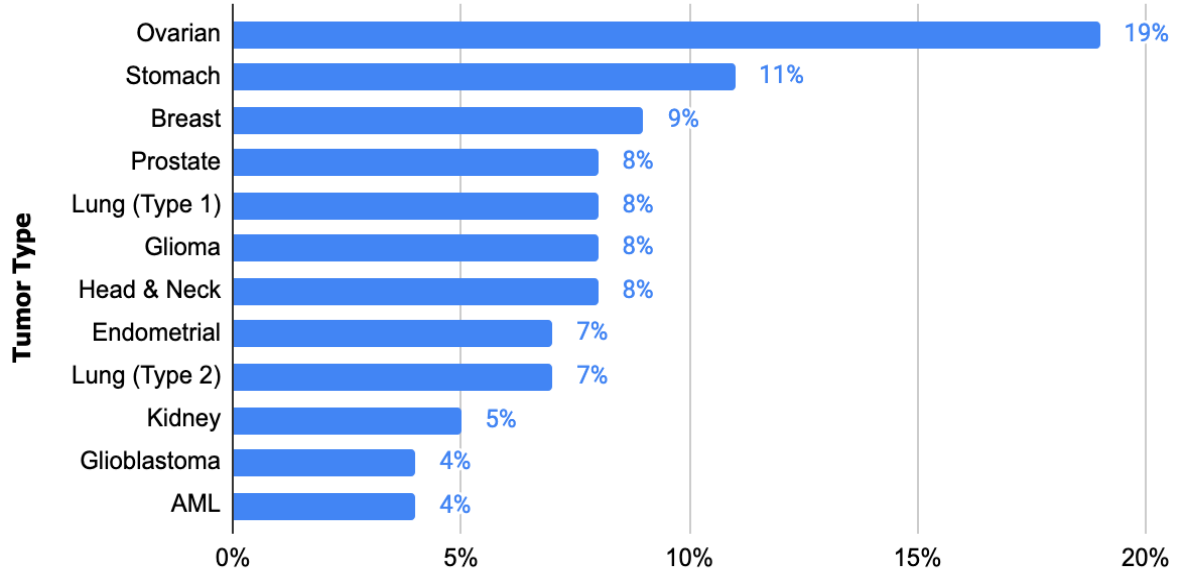


Figure 5: Percentage of Tumors from Inherited Mutations

Somatic Mutations: Somatic mutations are acquired genetic alterations that occur during a person's lifetime, often due to exposure to environmental factors such as UV radiation, tobacco smoke, or certain chemicals. These mutations can disrupt cellular pathways involved in regulating cell growth, division, and death, leading to the development of cancer.

Genetic Susceptibility: While certain inherited mutations directly contribute to cancer risk, other genetic variations may increase susceptibility to environmental carcinogens or modify the body's ability to repair DNA damage. These genetic factors can influence an individual's likelihood of developing cancer in response to specific environmental exposures.

5. FDA APPROVED DRUGS FOR CANCER TREATMENT

There are numerous FDA-approved drugs for the treatment of various types of cancer.

Table 2: FDA Approved Anti-Cancer Drugs

Chemotherapy Agents	Targeted Therapies	Immunotherapy	Hormonal Therapies
Paclitaxel	Imatinib (Gleevec): Targets BCR-ABL in chronic myeloid leukemia (CML)	Pembrolizumab (Keytruda): PD-1 inhibitor in melanoma, NSCLC, and head and neck squamous cell carcinoma (HNSCC)	Tamoxifen
Docetaxel	Trastuzumab (Herceptin): Targets HER2/neu in breast cancer	Nivolumab (Opdivo): PD-1 inhibitor in melanoma, NSCLC, and renal cell carcinoma (RCC)	Anastrozole (Arimidex)
Doxorubicin	Rituximab (Rituxan): Targets CD20 in non-Hodgkin's lymphoma	Ipilimumab (Yervoy): CTLA-4 inhibitor in melanoma	Letrozole (Femara)
Cisplatin	Bevacizumab (Avastin): Targets VEGF in various cancers	Atezolizumab (Tecentriq): PD-L1 inhibitor in NSCLC, urothelial carcinoma, & triple-negative breast cancer	Fulvestrant (Faslodex)
Carboplatin	Erlotinib (Tarceva): Targets EGFR in non-small cell lung cancer (NSCLC)	Durvalumab (Imfinzi): PD-L1 inhibitor in NSCLC and bladder cancer	Leuprolide (Lupron)
Gemcitabine	Gefitinib (Iressa): Targets EGFR in NSCLC	Avelumab(Bavencio): PD-L1 inhibitor in Merkel cell & urothelial carcinoma	Degarelix (Firmagon)
Vinblastine	Lapatinib (Tykerb): Targets HER2/neu in breast cancer		Abiraterone (Zytiga)
Vincristine	Sorafenib (Nexavar): Targets multiple kinases in renal cell carcinoma (RCC) and hepatocellular carcinoma (HCC)		Enzalutamide (Xtandi)

Methotrexate	Sunitinib (Sutent): Targets multiple kinases in RCC, gastrointestinal stromal tumors (GIST), and pancreatic neuroendocrine tumors (pNET)		
Fluorouracil	Palbociclib (Ibrance): CDK4/6 inhibitor in breast cancer		

These drugs are used alone or in combination with other treatments such as surgery, radiation therapy, or other drugs, depending on the type and stage of cancer. The landscape of cancer treatment is rapidly evolving, with new drugs and therapies continuously being researched and approved for clinical use.

6. MARKET POTENTIAL AND RECENT PATIENT POPULATION IN CANCER

The oncology/cancer drugs market size was valued at USD 138.41 billion in 2022 and is projected to hit around USD 401.31 billion by 2032, growing at a CAGR of 11.43% from 2023 to 2032 Figure 6).

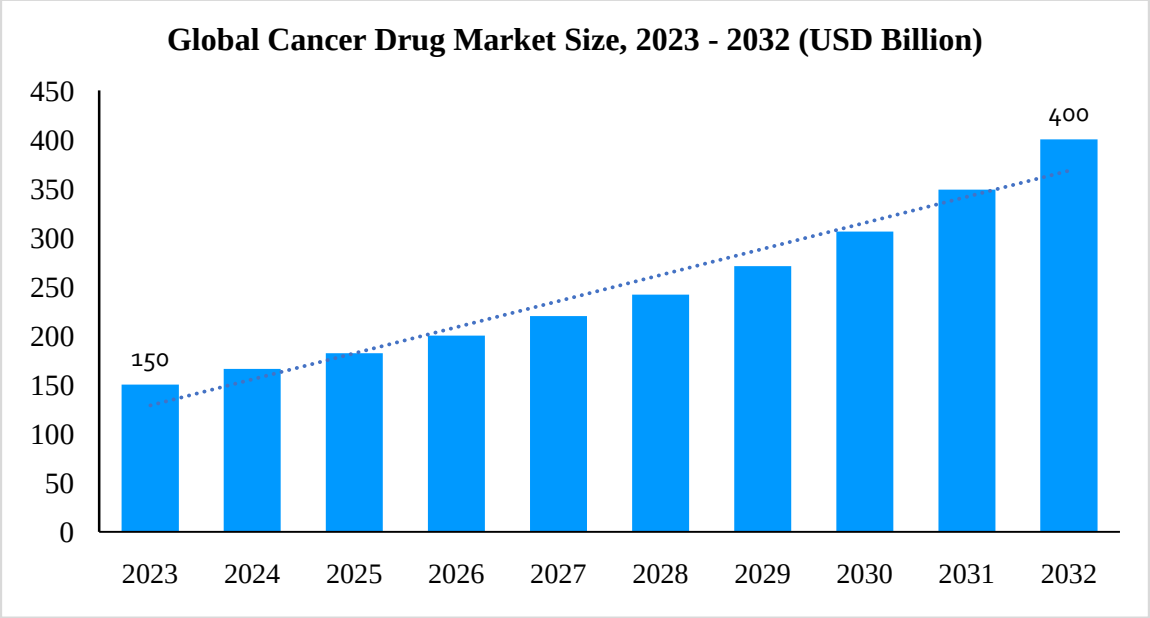


Figure 6: Global Cancer Drug Market Size

Figure **7** indicates the number of global cancer cases and deaths in 2022. Based on the indication, lung cancer is the most prominent type of cancer that affects the majority of the global population. According to the International

Agency for Research on Cancer, around 1.8 million deaths were recorded due to lung cancer in 2022. Lung cancer is the leading cause of the cancer deaths that accounts for around 18% of the global cancer deaths.

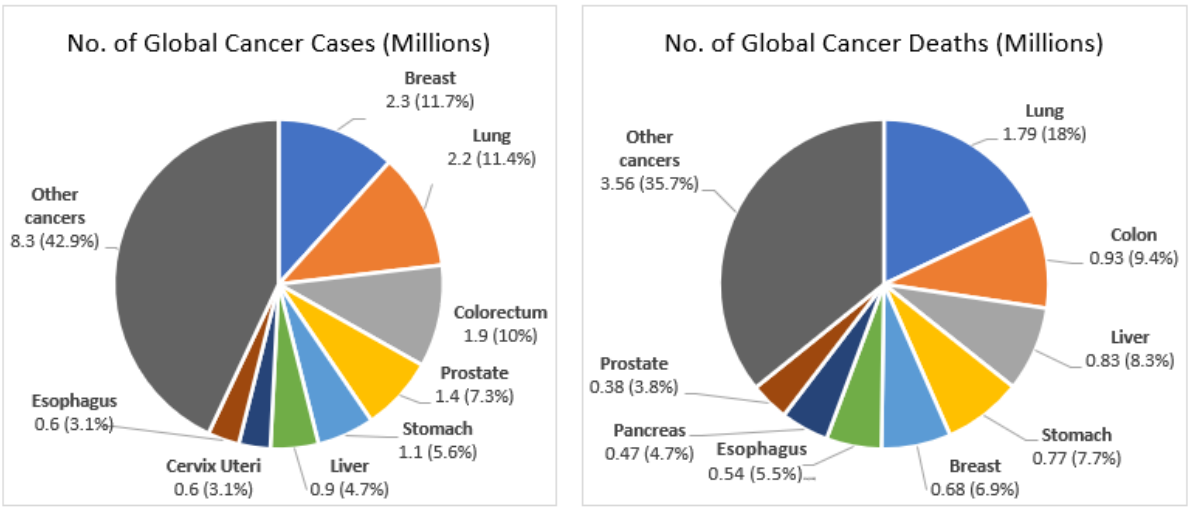


Figure 7: Number of Global Cancer Cases and Deaths

The rapidly rising case of breast cancer amongst the female population is driving the growth of this segment. According to the International Agency for Cancer Research, around 2.3 million or 11.7% of the new cancer cases reported as the breast cancer in 2022. The breast cancer has surpassed the lung cancer as the most diagnosed type of cancer across the globe.

7. RENOVEL APPROACH FOR ANTI-CANCER DRUG DISCOVERY

RENOVEL Innovations has developed its own library of molecules from natural product resources including Indian Ayurvedic herbs. A number of herbal ingredients have been used for the treatment and management of cancer in Ayurvedic medical practices. Table 3 represents recently synthesized 40 new orally active anti-cancer molecules.

Table 3: Orally Active Anti-Cancer Molecules Synthesized by RENOVEL

RNV-3001	RNV-3009	RNV-3017	RNV-3032	RNV-3072
RNV-3002	RNV-3010	RNV-3018	RNV-3033	RNV-3073
RNV-3003	RNV-3011	RNV-3019	RNV-3034	RNV-3074
RNV-3004	RNV-3012	RNV-3020	RNV-3067	RNV-3075
RNV-3005	RNV-3013	RNV-3021	RNV-3068	RNV-3076
RNV-3006	RNV-3014	RNV-3029	RNV-3069	RNV-3077
RNV-3007	RNV-3015	RNV-3030	RNV-3070	RNV-3078
RNV-3008	RNV-3016	RNV-3031	RNV-3071	RNV-3079

Cancer cell lines are widely used as *in vitro* assay systems, which have a significant role in early drug discovery for screening of compounds. The data generated from cell line studies is vital for further testing in animal models prior to clinical development.

The synthesized compounds were screened for various human cancer cell lines using Promega CellTiter-Glo 2.0 to generate initial efficacy data and growth inhibition along with cytostatic and cytotoxic responses. A heatmap of compounds activity was generated to identify potential active molecules. A typical heatmap pattern is shown in Figure 8 using single agent and cell lines.

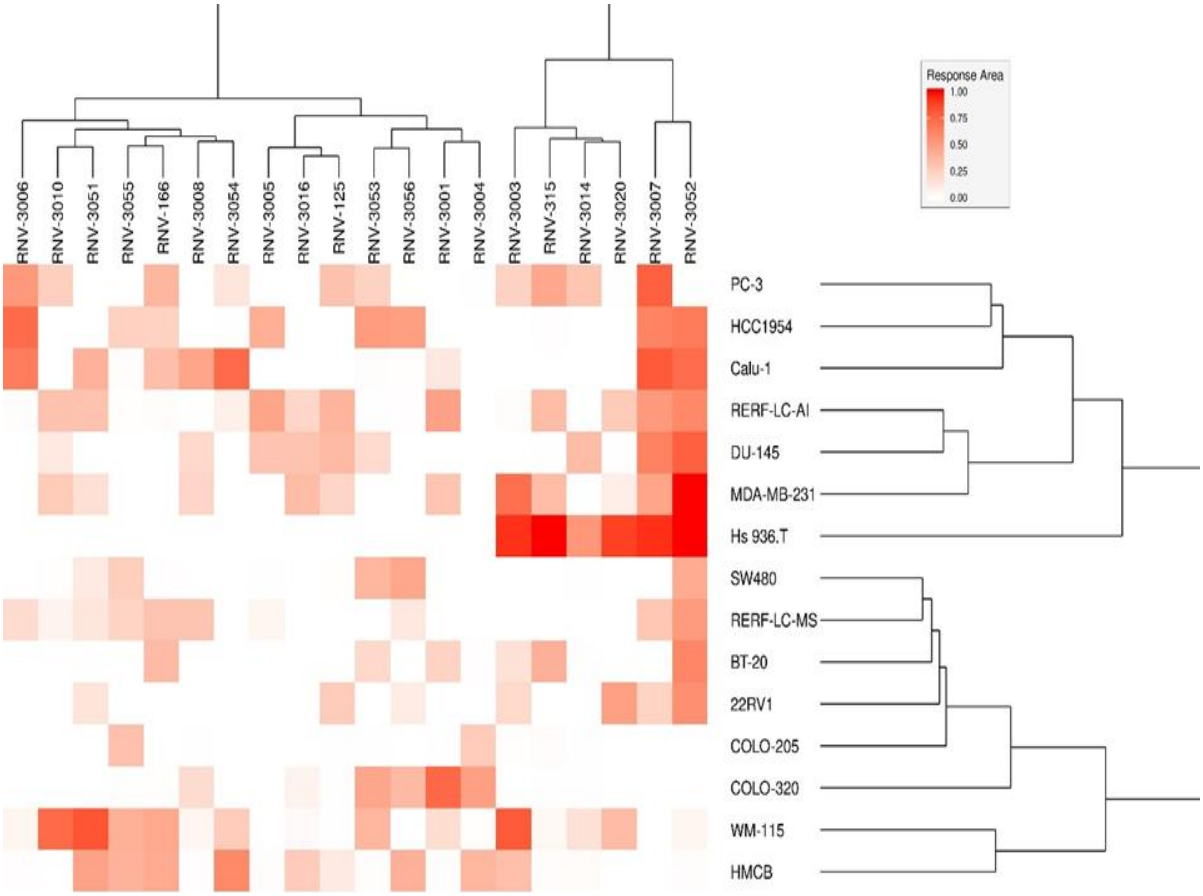


Figure 8: Heat Map for Screening of RENOVEL Anti-Cancer Molecules

In parallel, a box whisker plot was generated showing response of a single molecule by various tissue types, as shown in Figure 9. The breast, colorectal, lung, prostate, and skin tissues were used to screen compounds. Cell lines are sorted by median response for each tissue type.

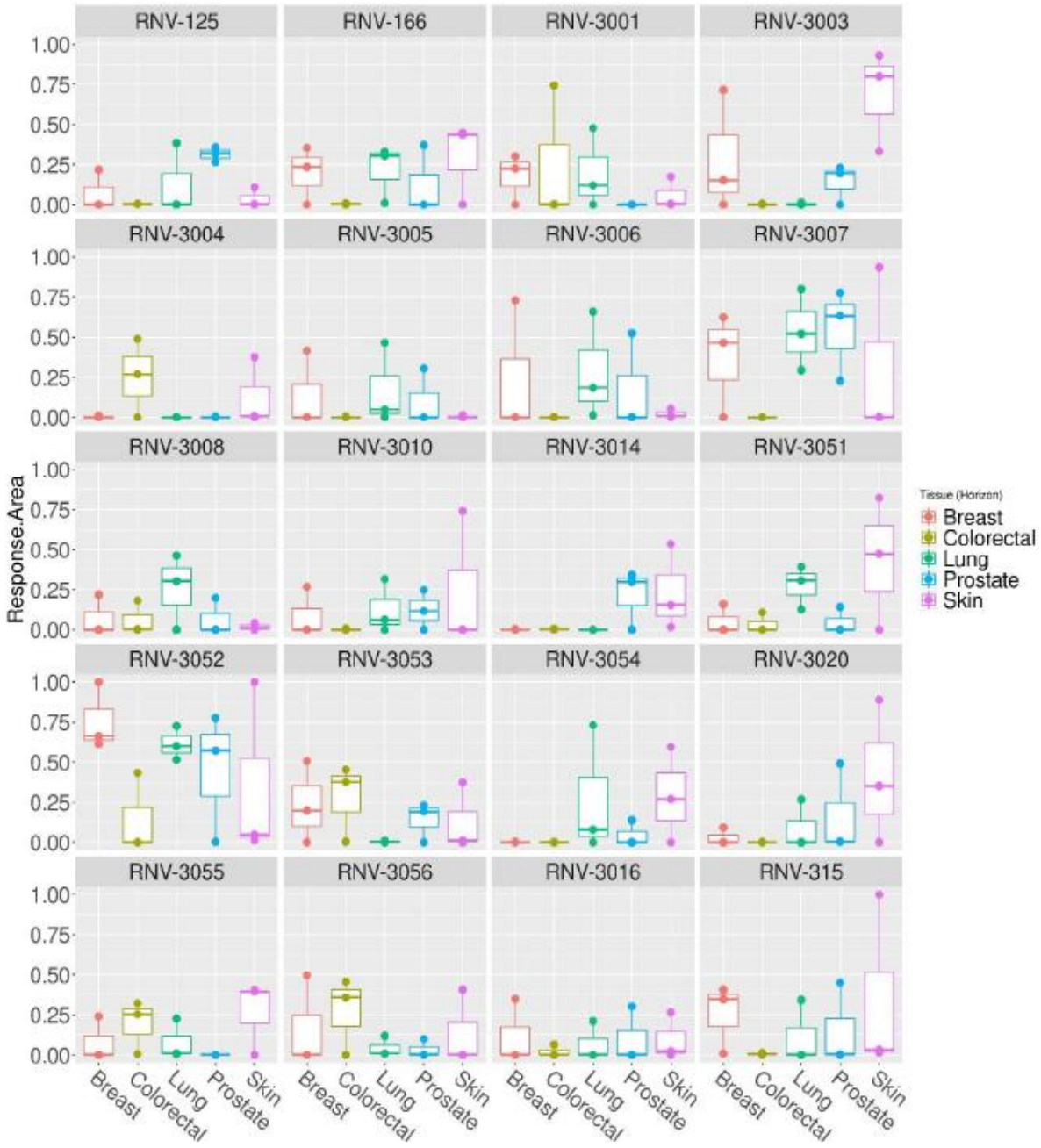


Figure 9: Box Whisker Plots Showing Single Agent Response by Tissue Type

8. ANIMAL MODELS FOR ANTI-CANCER LEAD MOLECULES

A number of animal models are being used to develop anti-cancer lead compounds. Experimental animal models allow for conduct of in vitro analysis, and together confer more compelling results. Mice models for preclinical testing of novel therapeutic strategies for an ultimate goal towards clinical implementation are of utmost importance in current research practice. These models generally serve as bridges between in-vitro testing and the heterogeneous makeup of a living organism whereby numerous interconnected cellular entities within a microenvironment will sustain a pathological state.

Mice animal models are widely used in cancer research due to their low cost, availability, and diversity of immunocompetent and immunodeficient strains.

For oncology research, the most widely used models consist of immunocompetent or immunocompromised mice transplanted subcutaneously or orthotopically with syngeneic and xenografted tumors; their use is mainly justified by their low cost and ease of generation. However, in a clinical practice, the malignant environment within an oncological patient is far more complex.

Another type of models for cancer research used in preclinical settings is represented by transgenic mice, wherein tumor suppressor genes are downregulated or oncogenes are expressed preferentially via three main methods: DNA construct microinjection, retroviral infection, and "gene-targeted transgene" method.

Recently, in line with advances in immunotherapy for oncological research, humanized mouse xenograft models have been developed to functionally introduce the interplay between human cancer cells and human immune cells. These mice are transplanted with patient-derived xenografts, and also with CD34+ cells that will bring forward the interactions between a tumor and stromal/immune cells. Various syngeneic and xenograft mice models that are being used to evaluate in vivo efficacy are shown in Table 4.

Table 4: In vivo Cancer Mice Models

Syngenic Models	Human Xenograft Models
Syngeneic, Breast, 4T1	Xenograft, Bladder, UM-UC-3
Syngeneic, Breast, Orthotopic, 4T1-Luc	Xenograft, Brain, U87-MG
Syngeneic, Breast, Metastasis, 4T1	Xenograft, Brain, Orthotopic, U87-MG-Luc
Syngeneic, Colon, CT26.WT	Xenograft, Breast, BT-474
Syngeneic, Colon, MC-38	Xenograft, Breast, HCC-1428
Syngeneic, Kidney, Renca	Xenograft, Breast, JIMT-1
Syngeneic, Leukemia, L1210	Xenograft, Prostate, LNCaP clone FGC
Syngeneic, Lymphoma, A20	Xenograft, Prostate, PC-3
Syngeneic, Lung, KLN 205	Xenograft, Skin, A-431
Syngeneic, Lung, LL/2	Xenograft, Colon, HCT 116
Syngeneic, Melanoma, B16-F0	Xenograft, Colon, HT-29
Syngeneic, Melanoma, Metastasis B16-F0	Xenograft, Lung, NCI-H1975

9. FUTURE OF ANTI-CANCER DRUG DISCOVERY

Cancer research has made significant strides in recent years, with groundbreaking discoveries and innovative technologies shaping the landscape of oncology. Scientists and researchers worldwide are dedicated to unraveling the complexities of cancer, leading to improved diagnostics, treatments, and prevention strategies.

Immunotherapy Breakthroughs: Immunotherapy has emerged as a game-changer in cancer treatment. Recent developments focus on enhancing the body's immune system to recognize and destroy cancer cells. Checkpoint inhibitors, CAR-T cell therapy, and personalized cancer vaccines have shown remarkable success in various types of cancer, offering new hope to patients who previously had limited treatment options.

Precision Medicine and Genomics: Advances in genomics have paved the way for precision medicine, tailoring treatments based on an individual's genetic makeup. Liquid biopsies, which involve analyzing circulating tumor DNA, offer a non-invasive method for early cancer detection and monitoring treatment response. The ability to target specific genetic mutations has led to more effective and personalized cancer therapies.

Targeted Therapies: Targeted therapies continue to evolve, focusing on specific molecules or pathways involved in cancer growth. Small molecule inhibitors and monoclonal antibodies are designed to interfere with the signaling pathways that drive cancer progression. As researchers uncover more about the molecular mechanisms of different cancers, targeted therapies become increasingly precise and effective.

Liquid Biopsies for Early Detection: Early detection remains a critical factor in improving cancer survival rates. Liquid biopsies, which analyze circulating tumor cells or DNA in blood samples, offer a minimally invasive method for detecting cancer at its earliest stages. This approach is particularly promising for cancers with limited screening options, such as pancreatic and ovarian cancers.

Combination Therapies: Researchers are exploring the synergistic effects of combining different treatment modalities to enhance their efficacy. Combining immunotherapy with chemotherapy, radiation, or targeted therapies has shown promise in overcoming resistance and improving overall treatment outcomes. The era of combination therapies represents a multifaceted approach to tackling the complexities of cancer.

Recent trends in cancer research reflect a dynamic and rapidly evolving field. From immunotherapy breakthroughs to the integration of artificial intelligence, these advancements offer new avenues for cancer prevention, diagnosis, and treatment. As researchers continue to unravel the complexities of cancer biology, the future holds the promise of more effective and personalized strategies to combat this challenging disease. The collaborative efforts of scientists, clinicians, and technological innovators underscore the dedication to improving the lives of cancer patients worldwide.

10. ROLE OF ARTIFICIAL INTELLIGENCE IN CANCER DRUG DISCOVERY

Artificial intelligence (AI) plays a significant role in the discovery and development of anti-cancer drugs by accelerating the drug discovery process, optimizing drug design, and identifying novel therapeutic targets.

Drug Discovery and Repurposing: AI-driven algorithms can analyze large datasets of biological, chemical, and clinical information to identify potential drug candidates and repurpose existing drugs for cancer treatment. By mining vast databases of chemical compounds, genomic data, protein structures, and biomedical literature, AI algorithms can predict the likelihood of a compound's efficacy against specific cancer types and prioritize candidates for further investigation.

Target Identification and Validation: AI-powered platforms can analyze complex biological data to identify disease-specific molecular targets and pathways involved in cancer development and progression. By integrating genomics, transcriptomics, proteomics, and other 'omics data, AI algorithms can prioritize potential drug targets and validate their relevance in preclinical models, accelerating the drug discovery process.

Drug Design and Optimization: AI-driven computational models, such as machine learning and deep learning algorithms, can generate predictive models of drug-target interactions, predict compound properties, and optimize drug candidates for efficacy, safety, and pharmacokinetic properties. These computational approaches enable the rapid design and optimization of novel anti-cancer drugs with enhanced potency and selectivity.

Personalized Medicine and Biomarker Discovery: AI technologies enable the development of personalized cancer therapies tailored to individual patients based on their unique molecular profiles and treatment responses. By analyzing patient-derived genomic and clinical data, AI algorithms can identify predictive biomarkers of drug response, stratify patients into subgroups with distinct

treatment outcomes, and optimize treatment strategies for improved therapeutic efficacy and patient outcomes.

Drug Screening and High-Throughput Analysis: AI-driven platforms automate and streamline the process of drug screening and high-throughput analysis, enabling the rapid identification of lead compounds and evaluation of their biological activity against cancer cells. By integrating robotics, microfluidics, and AI algorithms, researchers can perform large-scale drug screening assays, identify promising drug candidates, and prioritize compounds for further preclinical and clinical development.

Drug Combination Therapy: AI-based approaches can optimize combination therapy strategies by analyzing drug interactions, synergies, and resistance mechanisms in cancer cells. By integrating multi-omics data and predictive modeling techniques, AI algorithms can identify synergistic drug combinations, overcome drug resistance, and enhance the therapeutic efficacy of anti-cancer treatments.

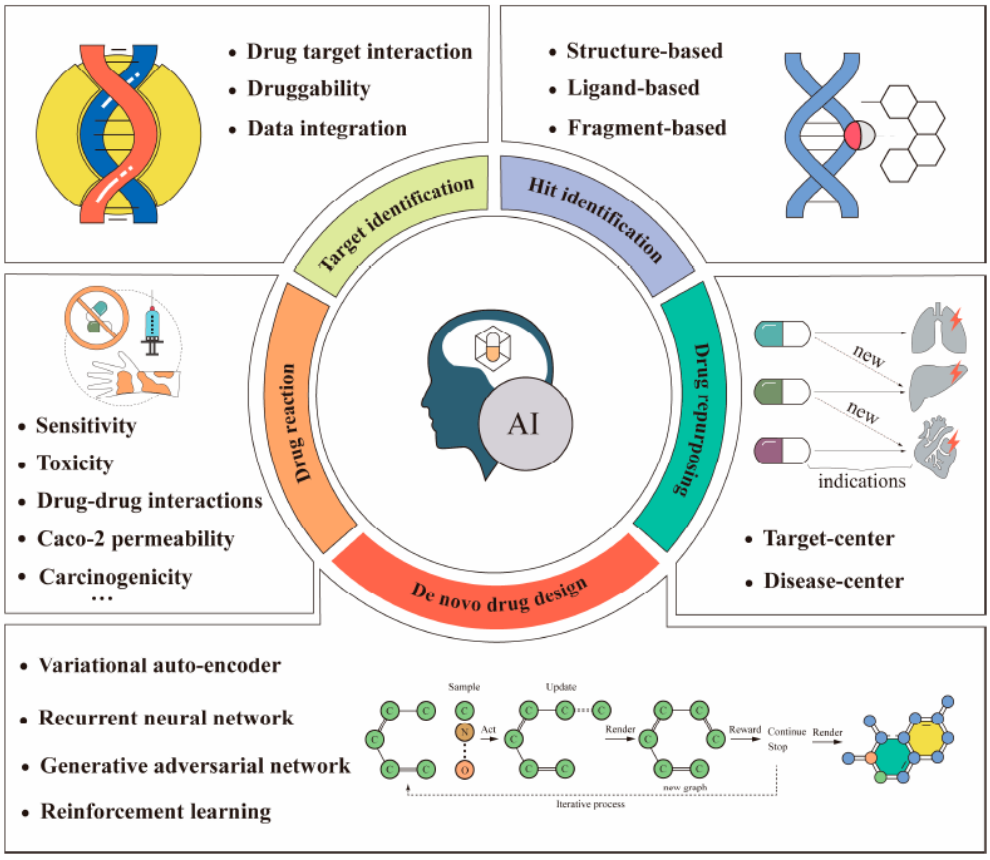


Figure 10: Some Applications of Artificial Intelligence in Anti-Cancer Drug Design

Source: Wang, L. et al; Advances of Artificial Intelligence in Anti-Cancer Drug Design: A Review of the Past Decade. *Pharmaceuticals* 2023; 16(2): 253.

Overall, AI-driven approaches hold great promise for accelerating the discovery and development of anti-cancer drugs, improving treatment outcomes, and advancing personalized cancer care. By leveraging the power of AI, researchers can harness the vast wealth of biological data to unlock new insights into cancer biology, identify novel therapeutic targets, and bring innovative treatments to patients more efficiently and effectively.

11. CONCLUSION

In general, established ancient natural product ingredients are considered relatively safe. The overview article gives some highlights on RENOVEL approach to discover new drugs for cancer treatment using ancient ayurvedic ingredients in combination with a library of creative natural product pharmacophores. The approach of RENOVEL is to find potential lead candidates with high safety margin that differentiate from typical screening of compounds used by traditional pharmaceutical organizations. Our approach is to design the compounds first and screen each compound for patentability before starting the synthesis process. This approach has proven track record of high success rate in other therapeutic areas for us. Development of such molecules from pre-clinical to Phase I and Phase II trials will bring new class of drug candidates for the treatment and management of major cancer cases world-wide.

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