

TO STUDY BIOACTIVE SMALL MOLECULE MARKET IN ONCOLOGY AND DIFFERENT AREAS

Dissertation Report submitted to



*For the partial fulfillment for the award of the degree of Master of Business Administration (MBA)
in Hospital and Health Management*

by

Dr. Prakshi Garg

(Batch-2020-2022)

Under the Supervision and Guidance of

Monika Chaudhary, Assistant Professor

DECLARATION BY STUDENT

I hereby declare that this dissertation title **“To study bioactive small molecule market in Oncology and different areas”: A Systematic Literature Review** is the bonafide record of my original research work. I declare that it has not been submitted to any other university or institution for the award of any degree or diploma. Information derived for the published or unpublished work of others has been duly acknowledged in the text.

Dr. Prakshi Garg

Date: 2/07/2022

CERTIFICATE

This is to certify that the dissertation title "**To study bioactive small molecule market in Oncology and different areas**": **A Systematic Review** of Literature is a record of the research work undertaken by Dr. Prakshi Garg in partial fulfillment of the requirements for the award of the degree of MBA (Hospital and Health Management from the IIHMR University, Jaipur under my guidance and supervision and his/her approach to the research study has been sincere, scientific, and analytical.

(Dr. Mahender Kumar)

Dean (Academics)

The IIHMR University, Jaipur

(Monika Chaudhary)

Assistant Professor

The IIHMR University, Jaipur

ACKNOWLEDGEMENT

A research project acts as a link between real-world experience and theoretical knowledge. With all that in mind, I researched a topic that would provide a wide overview of a new concept that emerged in India only a few years ago. The project's progress and completion required a great lot of guidance and assistance from many people, and I consider myself quite fortunate to have received this over the course of this work.

My explicable gratitude goes to Dr. Mahender Kumar (Dean of Academics) for constantly being approachable for student-related concerns.

I feel highly elated to keep on the timeline of my records to my university mentor Monika Chaudhary, Assistant Professor, IHMR university, Jaipur for her constant guidance and approachability. Her constant inspiration and encouragement helped me perform this research study in a very smooth manner.

It was an honour to be granted such an opportunity. I am thankful to all for their support for my dissertation work.

Date: 2 July 2022

Place: IIHMR University, Jaipur

Dr. Prakshi Garg

INDEX

S. No.	Table of Content	Page No.
1.	Abbreviation	6
2.	Introduction	7
3.	Bioactive small molecules	8
4.	Literature Review	9-10
5.	Study objectives & Methodology	11
6.	Research areas and applications	12-13
7.	Drivers, opportunities , restraints and challenges	14-16
8.	Future Trends	17
9.	Market Estimation	18
10.	Key Takeaways	19
11.	Conclusion	20
Reference		21

1. ABBREVIATION:-

BSM	Bioactive small molecules
NPs	Natural products
PROTAC	Proteolysis targeting Chimera
LYTAC	Lysosomal targeting Chimera
AbTAC	Antibodies targeting Chimera
HATs	Hypoxanthine , Aminopterin , Thymidine
AI	Artificial Intelligence
CVD	Cardiovascular diseases

2. INTRODUCTION

Health Sector is one of the few sectors which has been spreading its arms in different areas. One of the critical areas is research. Research in healthcare is directed towards improving healthcare. It helps doctors to get a more refined picture of human health and disease. This helps healthcare workers to learn better ways to prevent and treat diseases.

Health research is often referred to as medical research or clinical research as all the research is inclined towards improving human health. Health research is done in many forms like clinical trials on human beings or in the laboratory to target some specific sites for treatment of diseases. These different forms of health research led to some amazing discoveries, the development of new therapies and significant improvements in healthcare and public health.

Research done for discovering new medicines or drug targets is done using certain modalities like small molecules, antibodies, antibody drug conjugates and cells either in combination or alone. Some of the fields wherein these molecules have played a pivotal role in treatment are oncology, cardiovascular diseases as well as some other chronic diseases.

Research helps in fair use of existing tools and medicines for the treatment of diseases. Also the research lead to the decreasing cost to treat chronic, debilitating diseases and improving early detection of diseases. These researches ultimately improved the quality of life of the patients .Also medical research helps in finding out health statistics , mortality and morbidity which is required for national and local planning.

Today many technological innovations like AI and Machine Learning has aided in the research field

3. BIOACTIVE SMALL MOLECULES

3.1 DEFINITION - Bioactive small molecules refers to the class of molecules which has low molecular weight and are used for various life science research purposes. They do not have mass more than a one kilodalton. These include enzyme substrates , activators and inhibitors , cell signaling modulators etc which aids in various life science researches . They are basically used in screening purposes for investigating function of macromolecule targets

3.2 TYPES -

3.2.1 Naturally Occurring BSM - These are the biomolecules which are obtained from the natural occurring sources . Example - Secondary metabolites

3.2.2 Synthetic BSM - These are basically obtained in the laboratory by performing different researches using different compounds . Example - Antiviral drugs

3.3 USES OF BIOACTIVE SMALL MOLECULES -

3.3.1 - They are used for various research purposes by being used as a chemical probe . These chemical probes bind to target especially protein and alters the function of this target within the biological system, hence producing the required effects .

3.3.2 - They are also being used as therapeutic agents to treat some deadly diseases like cancer , CVD diseases .

3.3.3 They are also being used as pesticides in farming

3.3.4 - They are also being used as cell Signaling molecules

4. LITERATURE REVIEW

4.1 Role of Small Molecule Targeted Compounds in Cancer (Targeted cancer, 22)

Small molecules can alter the tumor activity by binding to the target protein. They can be even administered as tablets and in spite of this, they do not alter the activity of genes, hence no altered immune response. Small molecules can even act as enzyme inhibitors as sometimes they inhibit the catalytic activity of enzymes by binding to them. And some small compounds act by binding to the receptor and activate them. Prostate carcinoma is being treated in this way.

4.2 A Novel Sulfonyl-Based Small Molecule Exhibiting Anti-cancer Properties (Novel Sulfonyl Small molecule, 2022)

Phenotypic screening is one of the methods to identify novel bioactive small molecules. Some compounds possess immuno-modulatory properties and sulfonyl containing hit. These compounds induce apoptosis in human cancer cells. These compounds are basically identified by HTS assay.

4.3 Identification of Bioactive Small Molecule Inhibitors of Separase (Mayer, 2022)

Aneuploidy is associated with deregulated separase activity which is the major characteristic of mostly human cancer. For identifying the small molecules which are capable of inhibiting Separase, highly sensitive assay is established to quantify separase activity in cells. In vitro assays confirmed that these compounds inhibit separase but do not effect any other protein related to separase like caspase & CD-clan protease. When performed compound treatment, HeLa cells with compromised separase activity reflected chromosome segregation defects. So these studies reflect that separase inhibiting compounds serve as lead compounds.

4.4 Bioactive Natural Small Molecule-Tuned Coassembly of Photosensitive Drugs for Highly Efficient Synergistic and Enhanced Type I Photochemotherapy

Self assembling Natural small molecules have gathered much attention as they possess anti cancer properties. With green and facile supramolecular strategy, a series of carrier-free terpenoid was developed which aids in enhanced and synergistic photodynamic/chemotherapy. These molecules possess favourable therapeutic features possessing synergistic, enhanced and secure combinatorial cancer efficacy along with highly efficient tumor ablation.

4.5 Simultaneous and controlled release of two different bioactive small molecules from nature inspired single material (Manna, 2022)

Controlled release of multiple bioactive molecule from same bioactive matrix is challenging. By using one step covalent and gelation of single polymer, biocompatible polymeric material is synthesized. These polymeric loaded small molecules displays bulk wettability properties and are capable of co-release of two different biomolecules. These biomolecules are capable of inhibiting cancer cell proliferation. These molecules in near future are capable of aiding in more biomedical applications.

4.6 Small Molecules Targeting HATs, HDACs, and BRDs in Cancer Therapy (Won, 22)

Histone acetylation modification has played the very crucial role in tumorigenesis . Some epigenetic regulations mechanisms has vital involvement in development and prognosis of cancer . So drugs targeting epigenetic regulation are new innovation for cancer treatment . Many active small molecules those who target histone acetylation regulatory enzymes or proteins like HATs , HDACs and BRDs , they have restoring protein levels to normal .

4.7 A small molecule strategy for targeting cancer stem cells in Hypoxic Microenviornments (Markossian, 2022)

Breast cancer comprises of heterogenic subpopulations out of which some cells are problematic . These cells are known as BCSCs and are solely responsible for recurrence . They are more prevalent in oxygen free environment which is majorly responsible for proliferation and stemness of these cells . There are some small molecules which targets these cells by decreasing CSC migration and lowering tumorigenesis.

5. STUDY OBJECTIVES AND METHODOLOGY

5.1 Objectives - The major study objective is to explore the uses of the Bioactive small molecules .

1. To define and describe the research areas and applications for using bioactive small molecules in Oncology and other areas
2. To provide detailed information regarding the major factors and technology influencing Bioactive small molecule market
3. To enlist the drivers , opportunities , restraints and challenges associated with current use as well as future use of bioactive small molecules
4. To estimate the future growth of the market

5.2 Research Methodology - A detailed literature review was conducted , with search technique oriented in a way such that articles published between 2015 to 2022. All the required data was collected from various crucial websites , databases , Journals , publications and papers . 100 research papers were looked for this research , 34 were excluded as they do not have small molecules as their context . 30 papers were excluded as they do not have any relation to small molecules . 29 articles were not full text articles so remaining 7 articles are reviewed which satisfies all the requirements.

- a) **Research Question** - To study bioactive small molecule market in Oncology and different areas
- b) **Study type** - Secondary
- c) **Study Design** - Observational Descriptive study - Secondary
- d) **Inclusion Criteria** -
 - All relevant articles between 2015 to 2022
 - Articles including oncology and small molecules
 - Articles including qualitative and quantitative information of small molecule market
- e) **Exclusion Criteria** -
 - Articles published before 2015
 - Studies not including small molecule

6. RESEARCH AREAS AND APPLICATIONS OF BIOACTIVE SMALL MOLECULES

6.1 ONCOLOGY - Oncology is one of the most widely used application of bioactive small molecule.

- ✓ Alarming incidence , technological advancement in diagnostics and drug delivery through gene panels are some of the reasons for heightened focus on this area
- ✓ Bioactive small molecules are increasingly being used to identify new drugs , signaling pathways and novel delivery paradigms
- ✓ They are used as reference standards for modifying oncological therapeutics
- ✓ Also they are used to identify novel mechanism of action for tumor molecule targeted therapy
- ✓ They are used as chemical probes for target identification and to study oncology related pathways
- ✓ Compound libraries are used for screening and validating hits across cancer types

6.2 NEUROSCIENCES - The demand for innovative therapeutics have been increased due to increasing cases of neurodegenerative disease and neurological diseases

- ✓ Bioactive small molecules are used as reference standard to assess molecular structure or study modifications in iron chelators , dopamine agonists etc
- ✓ To understand inhibition of amyloid and other toxic proteins in Alzheimer's pathology
- ✓ These molecules are used as neuroprotectors in neurodegenerative diseases signaling pathways
- ✓ Also it has been used in neuromodulation - cell culture to understand how bioactive polyphenols are modified by gut microbiota before absorption into cells

6.3 GENE REGULATION - Gene regulation are driven by growth of genomics and targeted medicine.

- ✓ Enhancement of CRISPR gene editing in human cells using transforming factor signaling inhibitor - using bioactive small molecule to inhibit signaling pathway
- ✓ Identification and study of master metabolites through screening , that can control cell physiology
- ✓ They are used as chemical probes or in cell culture to study gene regulation , such as investigation of Tau Inhibitors in cell culture to understand pre-mRNA behaviour and impact on splicing

7 . DRIVERS , RESTRAINTS , OPPORTUNITIES AND CHALLENGES

7.1 DRIVERS AND OPPORTUNITIES

7.1.1 Advancement and rising application of chemical probes

- ✓ The growing field of genetic testing has enlarged the scope of chemical probes . These probes can selectively and potently modulate protein activity
- ✓ There are various types of probes like affinity based probes that demonstrates unique photo cross linking mechanism and effectively reduced background labeling
- ✓ Bioluminescent probes are expanding the scope of optical imaging of new targets and study reactive profiles
- ✓ Click chemistry - It is a technique which increased the usage in proteomic analysis and activity based protein profiling . They have increased usage in synthesis of drug screening libraries , DNA encoded libraries and modification of late stage drugs

7.1.2 Rising investment in development and utilization of bioactive small molecules

- ✓ R&D for bioactive small molecules are increasing , driven by increased use of targeted degradation techniques , demand for new modalities and targets and increased funding for research
- ✓ Development of Novel techniques such as targeted protein degradation (TPD) , PROTACs are revolutionizing the typical drug discovery modalities
- ✓ Also LYTACs , AbTACs and RIBOTAC will increase the adoption bioactive small molecules by expanding the scope of targeted degradation to intracellular , extracellular and membrane proteins

7.1.3 Rise in chronic diseases

- ✓ Cancer has been increasing and so oncology remains a significant issue for healthcare sector , so leading pharma and biopharma companies and universities are looking for bioactive small molecules with novel mechanisms of action
- ✓ Inhibiting oncolytic pathways through bioactive small molecules , designing a bioactive small molecule against cancerous non coding RNA are some of the applications where these molecules are used
- ✓ They are also used in areas of CVD , diabetes , neurodegenerative diseases as well as development of antibiotics

7.1.4 Emerging countries pose a hotbed for opportunities

- ✓ Countries like India and China pose strong growth opportunity for drug discovery
- ✓ Countries intend to stimulate R&D activities through increase in drug discovery and development
- ✓ China drug discovery space is buzz with potential of AI in drug design

7.1.5 Growing demand for drug repurposing

- ✓ Drug repurposes allows scientist to run screens against molecules to test activity against other targets
- ✓ The relatively low cost of screening lower failure rate and ability to enter into clinical trials work in favour repurposing drugs
- ✓ Some organisations have compound libraries have compound libraries intended for drug repurposing
- ✓ Libraries screening witnessed an astronomical boost during COVID-era

7.2 RESTRAINTS AND CHALLENGES

7.2.1 Challenges with natural product based drug discovery

- ✓ Natural product libraries are obtained from natural sources which sometimes are incompatible with conventional drug bases assays which makes identification , isolation and characterization of bioactive compounds of interest challenging
- ✓ Gaining IPR for unmodified NPs also pose hurdles due to inconsistent regulatory frameworks
- ✓ These possess time cost and labor intensive challenges

7.2.2 Negative impact of machine bias

- ✓ Synthetic access to novel and specific small molecules continue to remain bottleneck . Traditional techniques are not reliable due to data bias in machine learning algorithms
- ✓ Lack of sufficient negative data effect computational applications such as functional group variations and scaffold hopping that are used for hit expansion

7.2.3 Lack of skilled personnel

- ✓ The drug discovery sector is in dire need of an agile workforce to leverage opportunities and overcome technical challenges
- ✓ There is scarcity of skill sets needed to manage discovery , development and manufacturing processes

8. FUTURE TRENDS

8.1 DNA Encoded libraries and fragment based libraries

- ✓ DNA encoded library have emerged to become crucial technology platform for ligand discovery and target based small molecule screening
- ✓ The availability of cost effective NGS and nascent developments in DEL-compatible chemistry are some of the crucial growth drivers for DEL as they join multi billion compound library category
- ✓ Developments in NMR is also driving growth of fragment based lead/drug discovery

8.2 Increasing applications of CADD

- ✓ CADD has been gaining traction , posing strong competition to existent HTS and HCS techniques
- ✓ The advancement is aiming at achieving faster , more efficient and more accurate screening and discovery of molecules . This is also driving synthetic methodologies in exhibiting complicated structural architectures and detailed chemical features
- ✓ With chemical libraries shooting beyond billion molecules , there is need for more efficient virtual screening methods

9. MARKET ESTIMATION -

- ✓ The Global market for Bioactive small molecule market is estimated to be 350 USD Million which is expected to grow and will generate a revenue of around 450 USD Million
- ✓ The CAGR for this market is expected to lie between 3%-4%
- ✓ Further , this market will expand into diagnostics , Academia , biotech and pharma and will fulfill different purposes
- ✓ North America accounts for about 53% bioactive small molecule market making it growth conducive market for drug discovery and application of bioactive small molecules within it
- ✓ Many countries have fueled market growth by recent establishment of screening based drug discovery organization and industry academia collaboration to promote drug discovery
- ✓ Aggressive AI adoption and increasing number of local bioactive molecule suppliers and exploding growth of pharma/biotech companies in the region
- ✓ Academic institutions have significant share of research in bioactive small molecules
- ✓ Diagnostic is another important sector

10. KEY TAKE-AWAYS

- ✓ Growth rate for this market is about 2.0-3.0%
- ✓ Expanding applications of chemical probes and PROTACs/LYTACs etc are some of the key growth contributing factors
- ✓ The important reason which restricts research process are limited negative controls
- ✓ Oncology remains one of the very important research areas for bioactive small molecules
- ✓ They also hold key importance in uses like reference standard and invivo studies

11. CONCLUSION

This research was conducted to find out the possible areas of research and application of bioactive small molecules as they have vast uses in the research areas , diagnostics , pharma and biopharma sector . Traditionally large molecules were used to treat diseases like cancer , CVD etc but now small molecules are also playing very significant role in the treatment . Traditional methods of research were surpassed by new methods like AI , HTS which allows multiple molecules to be screened simultaneously at same time . So lastly Biomolecules are the future of the drug industry.

BIBLIOGRAPHY

- Beck, H. (22, June 28). *Small molecules:Drug Discovery*. Retrieved from Science direct:
<https://www.sciencedirect.com/science/article/pii/S1359644622000733>
- Lemurell, M. (22, June 27). *Next generation therapeutics*. Retrieved from AstraZeneca:
<https://www.astrazeneca.com/r-d/next-generation-therapeutics/small-molecule.html>
- Manna, U. (2022, June 27). *Two different biomolecules*. Retrieved from PubMed:
<https://pubs.rsc.org/en/content/articlelanding/2018/tb/c8tb02406e>
- Markossian, S. (2022, June 28). *Screening for Genetic Diseases*. Retrieved from Annual Reviews:
<https://www.annualreviews.org/doi/10.1146/annurev-genom-083117-021452>
- Mayer, T. U. (2022, June 28). *Separase Activity*. Retrieved from PubMed:
<https://pubmed.ncbi.nlm.nih.gov/31553567/>
- Novel Sulfonyl Small molecule*. (2022, june 26). Retrieved from Frontiers:
<https://www.frontiersin.org/articles/10.3389/fphar.2020.00237/full>
- Targeted cancer*. (22, June 26). Retrieved from Frontiers:
<https://www.frontiersin.org/articles/10.3389/fcell.2021.694363/full>
- Won, M. (22, June 27). *Targeting Breast Cancer*. Retrieved from PubMed:
<https://pubs.acs.org/doi/10.1021/jacs.1c03875>