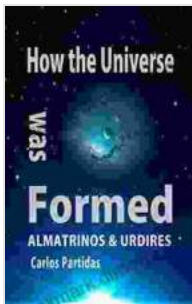


# Almatrinos Urdires: Unraveling the Chemistry of Diseases

## : The Ever-Evolving Landscape of Health and Disease

The human body, a marvel of biological complexity, is an arena of intricate chemical processes that determine our health and well-being.

Understanding these processes is paramount in comprehending the nature of diseases and developing effective treatments. Almatrinos Urdires: The Chemistry of Diseases emerges as a beacon of knowledge, shedding light on the profound interplay between chemistry and human health.



### HOW THE UNIVERSE WAS FORMED: ALMATRINOS & URDIRES (The Chemistry of Diseases Book 8) by Voltaire

★★★★★ 5 out of 5

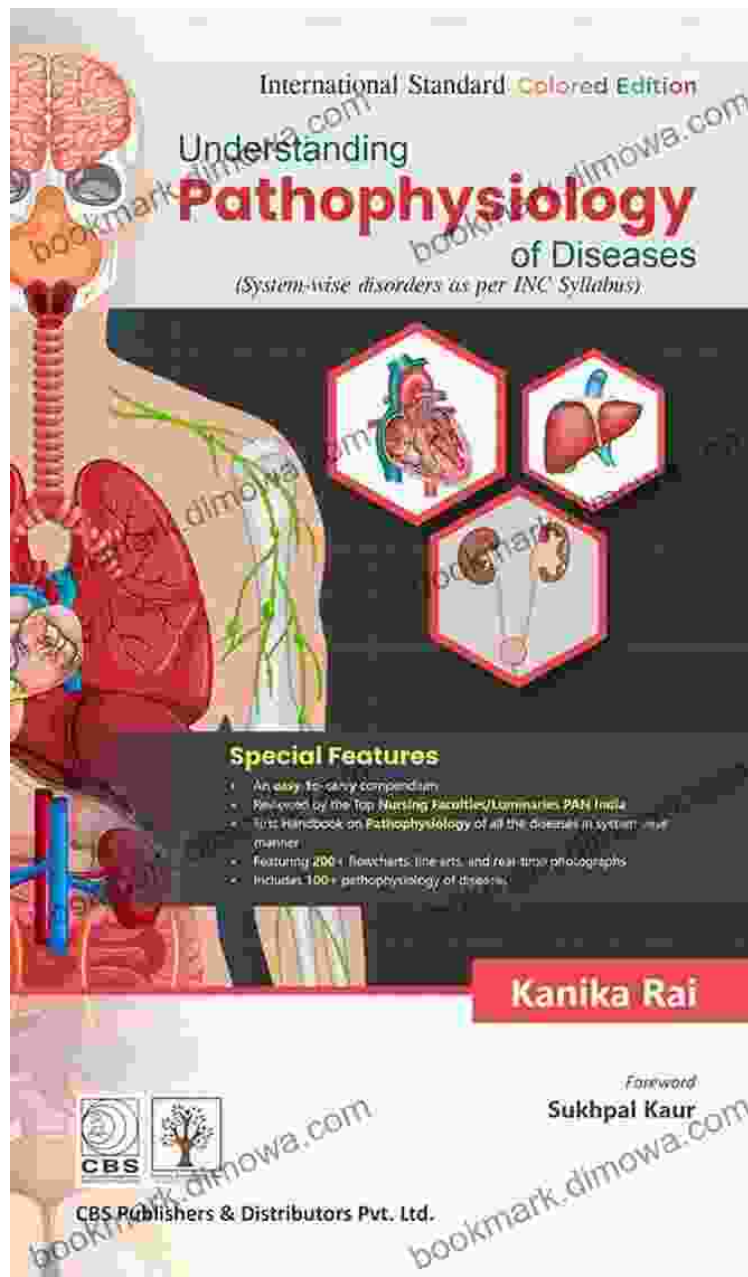
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## Chapter 1: Biochemistry: The Foundation of Life and Disease

This chapter embarks on a journey into the realm of biochemistry, the science that deciphers the chemical basis of life. Readers are introduced to

the building blocks of cells, the molecules that drive essential processes, and the intricate dance of enzymes that orchestrate chemical reactions. Understanding these fundamental principles forms the cornerstone for comprehending the molecular mechanisms underlying diseases.



## Chapter 2: Pathogenesis: The Genesis of Diseases

Moving beyond the foundations of biochemistry, Chapter 2 delves into the realm of pathogenesis, the study of disease development. Readers gain insights into how genetic mutations, environmental factors, and infectious agents disrupt normal cellular processes, leading to the onset of various diseases. This chapter provides a comprehensive examination of the complex factors that contribute to disease etiology.

### **Chapter 3: Disease Chemistry: Deciphering the Molecular Basis of Afflictions**

The core of this remarkable text lies in Chapter 3, where the chemistry of specific diseases takes center stage. From the molecular underpinnings of cancer to the intricate workings of cardiovascular ailments, readers embark on a journey through the biochemical landscapes of various diseases. This chapter not only enhances understanding of disease mechanisms but also paves the way for targeted therapeutic interventions.

# OPEN Unveiling the molecular basis of lobeline's allosteric regulation of NMDAR: insights from molecular modeling

Chandran Remya<sup>1</sup>, E. J. Varlyar<sup>2</sup>, R. V. Omikumar<sup>1</sup>, C. Sadasivan<sup>2,3</sup> & X. V. Dileep<sup>2,3</sup>

Neurological and psychiatric disorders contribute significantly to the global disease burden, adversely affecting the quality of life for both patients and their families. Impaired glutamatergic signaling is considered to be a major cause for most of the neurological and psychiatric disorders. Glutamate receptors are over-activated in excitotoxic conditions, leading to dysregulation of  $Ca^{2+}$  homeostasis, triggering the production of free radicals and oxidative stress, mitochondrial dysfunction and eventually cell death. Excitotoxicity primarily results from the overactivity of NMDARs, a subtype of ionotropic glutamate receptors, due to their pronounced  $Ca^{2+}$  permeability and conductance characteristics. NMDAR antagonists are suggested to have therapeutic use as they can prevent excitotoxicity. Our previous studies demonstrated lobeline, an alkaloid, averts neuroprotective actions in excitotoxic conditions by blocking NMDAR. However, the atomic level interaction of lobeline with NMDAR was not characterized yet. Structural comparison of lobeline with a known NMDAR antagonist desiprondil, followed by molecular docking and dynamic simulations revealed that lobeline could bind to the desiprondil binding site i.e., in the heteroameric interface of GluN1-GluN2B subunits and exert desiprondil-like activities. By in silico structural guided modifications on lobeline and subsequent free energy calculations, we propose putative NMDAR antagonists derived from lobeline.

Glutamate, the main excitatory neurotransmitter in the brain, plays a pivotal role in many brain processes including perception and cognition in the brain. This response is generated when glutamate interacts with its receptors. However, the excessive activation of glutamate receptors can lead to neuronal dysfunction and excitotoxicity<sup>1,2</sup>. Excitotoxicity is a condition in the central nervous system (CNS) characterized by excessive neuronal death due to an increased influx of  $Ca^{2+}$  into the cell of post-synaptic animal and neuronal, primarily glutamate<sup>3</sup>. The excessive influx of glutamate is accompanied by the activation of ionotropic receptors and neurotoxic compounds like  $Fe^{2+}$  generated. Rapid excitotoxicity by glutamate, in turn, leads to cell death in ionotropic receptors that include N-methyl-D-aspartate (NMDAR), ionotropic  $\alpha$ -amino-3-hydroxy-5-methylisoxazole-4-propionate (AMPA) and kainate (KAR) receptors<sup>4,5</sup>. These ionotropic receptors are ligand-gated ion channels that form ion-conducting channels. The NMDAR receptor (NMDAR) plays a pivotal role in both the structure and function of the nervous system, as well as in learning<sup>6</sup>. The dysfunction of NMDAR receptors is linked to NMDAR-related neurological and developmental disorders and Huntington's<sup>7</sup>.

The NMDARs are calcium ( $Ca^{2+}$ ) ions by glutamate-gated ion channels that are expressed in the CNS and were initially activated by the  $Ca^{2+}$  ions due to their high permeability and conductance properties<sup>8</sup>. NMDARs have a unique binding site for which, initially, usually composed of two protein subunits, GluN1 subunits and NR2 subunits, forming GluN2A-43 subunits<sup>9,10</sup>. Subsequent activation of NMDARs by AMPA and KAR leads to  $Ca^{2+}$  influx and permeability changes. These processes are the basis of electrochemical signaling system in a cell, which underlies operations of neurons. The NMDARs contain a complex array of various proteins, including glutamatergic receptors, ion channels, and scaffolding of

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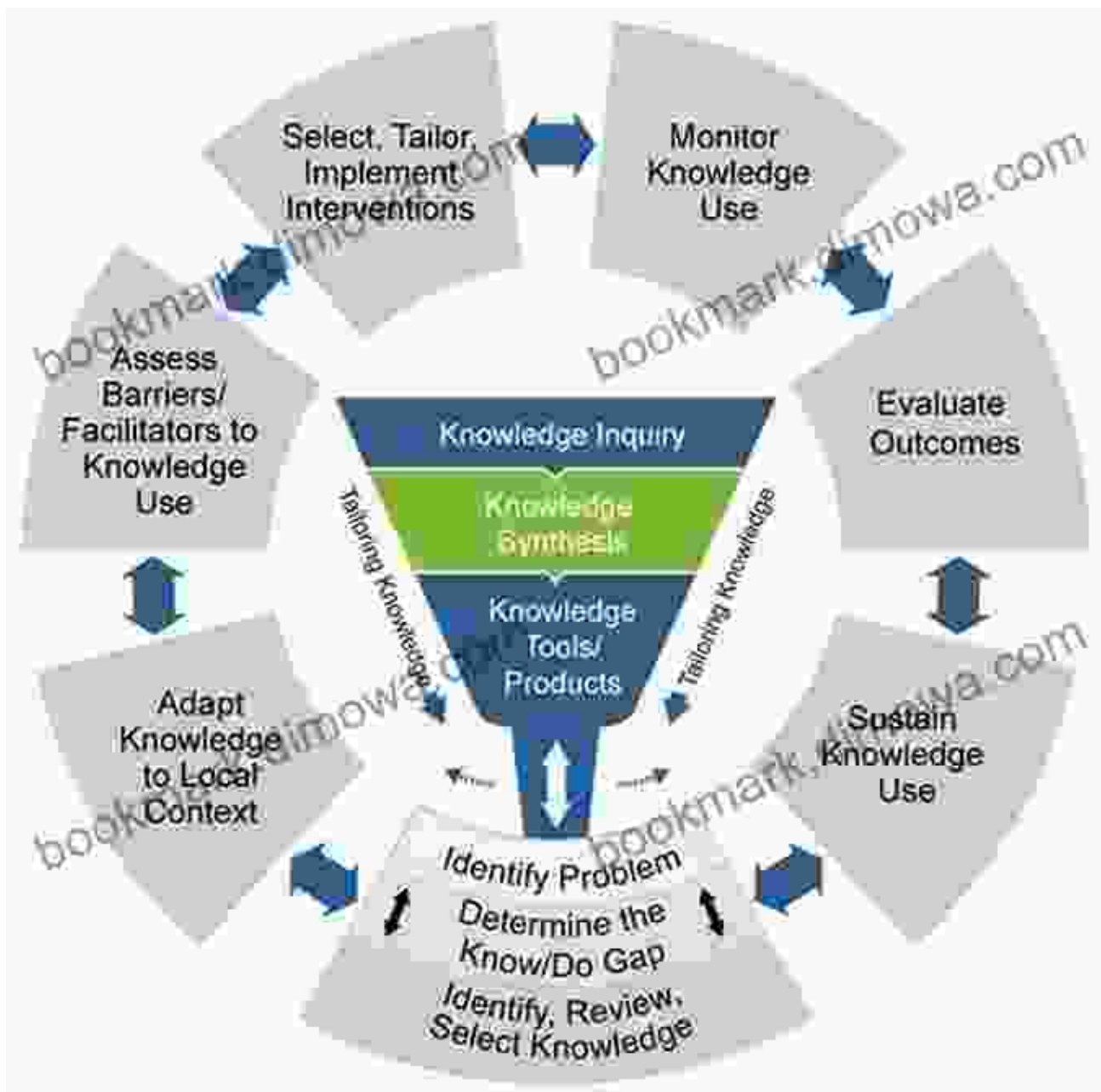
## Chapter 4: Pharmaceutical Development: Harnessing Chemistry to Combat Diseases

Armed with a deep understanding of disease chemistry, Chapter 4 explores the fascinating world of pharmaceutical development. Readers are taken through the intricate processes of drug discovery, design, and optimization.

They witness how chemistry plays a pivotal role in transforming scientific breakthroughs into tangible therapies that alleviate human suffering.

## **Chapter 5: Case Studies: Translating Knowledge into Practice**

To illustrate the practical applications of the knowledge gained throughout the book, Chapter 5 presents a series of in-depth case studies. These real-world examples showcase how the principles of disease chemistry guide the development of personalized treatments, revolutionizing patient care and improving health outcomes.



## : Chemistry as a Catalyst for Health and Healing

Almatrinos Urdires: The Chemistry of Diseases concludes by emphasizing the profound impact of chemistry on human health and well-being. This comprehensive text empowers readers with a holistic understanding of the interplay between chemistry and diseases, inspiring future generations to pursue careers in medicine, research, and drug development. By

unraveling the chemistry of diseases, we unlock the potential for transformative discoveries that will shape the future of healthcare.

### **About the Author: Almatrinos Urdires, a Visionary Biochemist**

Dr. Almatrinos Urdires, an accomplished biochemist and researcher, brings a wealth of knowledge and experience to this remarkable text. His decades-long dedication to understanding the chemistry of diseases has earned him international recognition and a reputation as one of the leading minds in the field. Dr. Urdires' passion for translating scientific discoveries into practical applications shines through in every chapter of this invaluable book.

### **Call to Action: Embark on a Journey of Discovery**

If you are a medical professional, a student aspiring to a career in healthcare, or simply an individual fascinated by the intricate workings of the human body, Almatrinos Urdires: The Chemistry of Diseases is an indispensable addition to your library. Its comprehensive content, engaging writing style, and practical applications will empower you to unravel the mysteries of diseases and contribute to shaping the future of healthcare.

Free Download your copy today and embark on a journey of discovery that will transform your understanding of human health and disease.

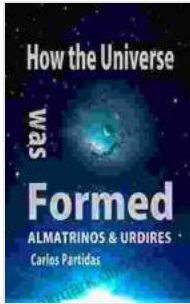
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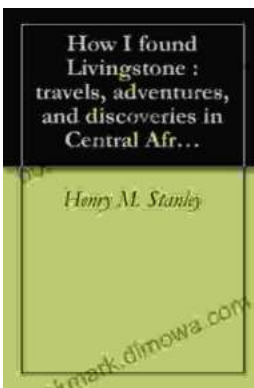
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