
Introduction

The first nucleoside triphosphate (NTP), adenosine triphosphate (ATP), was discovered by Karl Lohmann in 1929. Some years later, its structure was clarified, and Alexander Todd synthesized ATP chemically in 1948. A major role of ATP is supplying the needed energy to synthesize the many thousands of macromolecules that a cell needs to exist. ATP is described as the "universal currency of energy" in the cell and functions as a carrier of energy in all living organisms from bacteria and fungi to plants and animals, including humans. The actual power source is the phosphate tail of ATP. Available energy is contained in the bonds between the phosphates and is released when they are hydrolyzed. Usually, only the outer phosphate is removed to yield energy and the nucleotide diphosphate. Although ATP is the main energy carrier in the cell, other energized nucleotides containing thymine, guanine, uracil, and cytosine are utilized. Nucleoside diphosphate kinase transfers energy contained in a nucleoside triphosphate (commonly ATP) to a nucleoside diphosphate, such as guanosine diphosphate (GDP), to form guanosine triphosphate (GTP).

Nucleoside triphosphates are utilized by a family of polymerases during the synthesis of nucleic acids on preexisting nucleic acid templates, assembling RNA from ribonucleotides, or DNA from deoxyribonucleotides. Polymerase chain reaction (PCR), a key technique in molecular genetics that permits the analysis of any short sequence of DNA (or RNA) in the test tube, relies on NTP. The PCR technology has greatly increased scientists' ability to study genetic material. Since its invention, PCR has revolutionized the way in which basic research and medical diagnosis are conducted.

Structurally, NTP consists of three main components: the nitrogenous base, the sugar, and a chain of three phosphate groups bound to ribose. Since the discovery of the first nucleotide and elucidation of its structure (ATP), scientists have synthesized various analogs of NTP modified at the base, sugar, or triphosphate chain. These compounds have served as valuable tools in the investigation of a variety of cellular processes for many years. Modification of the triphosphate chain has been mainly used to study enzymatic pathways, which results in hydrolysis or transfer of the phosphate from NTP to another molecule. Modification of sugar and base has served a number of different purposes, from pharmaceutical to diagnostic applications.

Structural analogs of nucleoside have diverse biological properties and therapeutic consequences. They comprise a diverse family of cytotoxic compounds, antiviral agents, and immunosuppressive molecules. Anticancer nucleoside analogs inhibit cellular DNA replication and repair, whereas antiviral nucleoside analogs inhibit replication of the viral genome. Nucleoside analogs are inactive prodrugs and require intracellular phosphorylation to their corresponding pharmacologically active triphosphate form.

A number of nucleosides are currently on the market (or may be marketed soon) for the treatment of various diseases. Presently, the backbone of effective antiretroviral therapy regimens for the treatment of HIV contains at least two nucleosides. Pyrimidine nucleoside analogs are essential components of hematological malignancy therapy and are also used in the treatment of solid tumors. Furthermore, immunosuppressive properties of these agents have been exploited for preventing rejection following transplant and for the treatment of nonmalignant disorders, including immunologic diseases and multiple sclerosis.

Due to their essential role in virtually all cellular processes, nucleotide analogs that facilitate tracking of global conformational changes in nucleic acids and nucleic acid complexes have been utilized extensively in cellular and molecular biology research. A variety of labeled nucleotides for molecular biology and cytogenetic applications, such as gene expression studies, mutation detection on arrays, microarrays, and *in situ* PCR and RT-PCR, have been developed and are commercially available.

Fluorescent labeled nucleotide analogs provide sensitive probes for studying the structure, dynamics, and interactions of nucleic acids. These analogs can be incorporated site specifically into oligonucleotides through standard automated synthetic procedures, allowing them to serve as sensitive probes of changes in the microenvironment that may result from variation in molecular interactions. A major advantage of fluorescent analogs is their similarity in chemical properties and molecular constitution to natural bases. In contrast to bulkier chromophores, they are incorporated into the oligonucleotides without introducing significant structural or chemical changes that might alter the measurement.

This book is the first dedicated to the field of nucleoside triphosphate and encompasses within its chapters the contributions of 18 scientists from academia as well as industry, each of whom has contributed to the field. The purpose of this text is to provide collective information on chemistry, physicochemical, and biological properties of natural and modified NTP, as well as their application in life sciences. In addition, we have included three chapters that review families of enzymes that depend on nucleotides for assembling DNA and RNA molecules and an appendix with supporting information.

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