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# The Role of Potassium in Metabolism: Cellular Mechanisms, Exercise Physiology and Pathophysiological Implications

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## *Abstract*

***Background:*** *Potassium is an intracellular cation and a critical determinant of cellular homeostasis, membrane potential, and metabolic activity. Its tightly regulated distribution between intracellular and extracellular compartments is essential for normal physiological function.*

***Objective:*** *This review aims to synthesize current knowledge on the role of potassium in metabolic regulation, with emphasis on cellular bioenergetics, acid-base balance, exercise physiology, and the metabolic consequences of hyperkalemia.*

***Methods:*** *A narrative review of foundational and contemporary literature in physiology, nephrology, and biochemistry was conducted, focusing on mechanisms of potassium homeostasis and its interaction with metabolic pathways.*

***Results:*** *Potassium is central to maintaining electrochemical gradients through $Na^+/K^+$-ATPase activity, a major consumer of cellular ATP. It modulates enzyme function, facilitates nutrient transport, and contributes to acid–base equilibrium. During metabolic acidosis, potassium shifts from the intracellular to extracellular compartment, impairing enzyme activity and metabolic efficiency. In exercise, transient potassium efflux from skeletal muscle increases extracellular potassium concentration, necessitating ATP-dependent restoration via $Na^+/K^+$-ATPase. Hyperkalemia disrupts membrane excitability, impairs metabolic processes, and is associated with systemic dysfunction, particularly in renal disease.*

***Conclusion:*** *Potassium plays an integral role in metabolism by linking ionic homeostasis with energy production and cellular function. Disruptions in potassium balance, especially hyperkalemia, have signif-*

*icant metabolic and clinical consequences, underscoring the importance of precise regulatory mechanisms.*

**Keywords:** Acid-base balance; Electrolytes; Hyperkalemia; Metabolism; Potassium.

## Abbreviations

**ATP:** Adenosine Triphosphate

## Introduction

Potassium is the most abundant intracellular cation and is essential for maintaining cellular function and systemic homeostasis. Approximately 98% of total body potassium is localized within cells, where it plays a fundamental role in establishing membrane potential and supporting metabolic processes (1,2). The steep gradient between intracellular and extracellular potassium concentrations is critical for nerve conduction, muscle contraction, and nutrient transport.

Metabolic processes are highly dependent on intracellular ionic conditions. Potassium contributes to the regulation of enzyme activity, substrate utilization, and adenosine triphosphate (ATP) generation. Consequently, disturbances in potassium homeostasis can profoundly affect metabolic pathways and physiological stability (3,4). This review examines the mechanisms through which potassium influences metabolism, with a focus on cellular energetics, acid-base balance, exercise physiology, and pathological conditions such as hyperkalemia.

## Methods

This study is a narrative review based on established and peer-reviewed literature. Sources were selected from journals in physiology, nephrology, and biochemistry, including Physiological Reviews, The New England Journal of Medicine, and Clinical Journal of the American Society of Nephrology. Classic and contemporary studies addressing potassium homeostasis, metabolic regulation, and exercise physiology were included. Emphasis was placed on mechanistic insights and clinically relevant findings.

## Cellular potassium homeostasis and metabolic regulation

$Na^+/K^+$-ATPase and bioenergetics: the $Na^+/K^+$-ATPase is the principal mechanism responsible for maintaining intracellular potassium concentration. This enzyme actively transports sodium out of and potassium into the cell, consuming ATP in the process (2,3).

This pump is a major determinant of cellular energy expenditure, accounting for a significant fraction of basal metabolic rate, particularly in excitable tissues such as skeletal muscle and neurons (5). By maintaining the electrochemical gradient, it enables secondary active transport mechanisms that are essential for nutrient uptake and metabolic activity.

Potassium and enzyme function: intracellular potassium influences the activity of numerous enzymes involved in glycolysis, oxidative phosphorylation, and protein synthesis (4,6). Variations in potassium concentration alter enzyme conformation and catalytic efficiency, thereby affecting metabolic flux. Additionally, potassium plays a role in ribosomal function and protein translation, linking it directly to anabolic processes.

Role in nutrient transport: the sodium gradient established by $Na^+/K^+$-ATPase drives the transport of glucose and amino acids into cells. Disruption of potassium balance impairs this gradient, reducing substrate availability for metabolic pathways and ultimately limiting ATP production (3,4).

## Potassium and acid-base balance

Mechanisms of ionic shifts in acidosis: acid-base disturbances significantly influence potassium distribution. In metabolic acidosis, excess hydrogen ions enter cells to be buffered, leading to a compensatory efflux of potassium into the extracellular space (6,7).

This process is mediated by ion exchange mechanisms, reduced $Na^+/K^+$-ATPase activity, and changes in membrane permeability.

Metabolic consequences: acidosis-induced potassium shifts reduce intracellular potassium levels, impairing enzyme activity and metabolic efficiency. Concurrently, low pH directly inhibits metabolic pathways, including glycolysis and mitochondrial respiration (7). These combined effects contribute to decreased ATP production and altered metabolic homeostasis.

## Potassium dynamics during exercise

Ionic fluxes in skeletal muscle: during muscle contraction, repeated depolarization leads to potassium efflux as part of the repolarization process (8).

This results in transient increases in extracellular potassium concentration, particularly in the interstitial space surrounding active muscle fibers (8,9).

Energy demand and recovery: the restoration of ionic balance requires increased $Na^+/K^+$-ATPase activity, stimulated by catecholamines and insulin. This process consumes significant amounts of ATP, linking potassium regulation directly to energy expenditure during exercise (5,8).

Role in muscle fatigue: elevated extracellular potassium reduces membrane excitability, impairing action potential propagation and excitation-contraction coupling. This contributes to muscle fatigue and decreased performance during prolonged or high-intensity exercise (9,10).

## Hyperkalemia, cardiac, renal and diabetes alterations

Effects on cellular excitability: hyperkalemia reduces the resting membrane potential, impairing the ability of excitable cells to generate action potentials. This effect is particularly critical in cardiac tissue, where it can lead to life-threatening arrhythmias (1).

Impact on metabolic processes: elevated extracellular potassium disrupts ion-dependent transport systems and enzyme activity, impairing cellular metabolism. Hyperkalemia is often associated with renal dysfunction, which further exacerbates metabolic disturbances by reducing the excretion of potassium and metabolic waste products (2).

Interaction with glucose metabolism: potassium influences insulin secretion and sensitivity. Alterations in potassium balance can impair glucose uptake and utilization, linking electrolyte imbalance with metabolic disorders such as diabetes (11).

## Discussion

Potassium serves as a critical integrator of metabolic and physiological processes. Its role extends beyond maintaining membrane potential to influenc-

ing enzyme activity, nutrient transport, and energy expenditure. The dynamic regulation of potassium during exercise and in response to acid-base disturbances illustrates its importance in maintaining metabolic stability.

The interplay between potassium and metabolism is particularly evident in pathological states. Hyperkalemia disrupts both cellular and systemic function, highlighting the importance of renal regulation and hormonal control. Future research should further explore the molecular mechanisms linking potassium homeostasis with metabolic diseases and therapeutic interventions.

## Conclusion

Potassium is essential for metabolic regulation, acting at the intersection of ionic balance and cellular energetics. Its influence on enzyme function, nutrient transport, and ATP utilization underscores its central role in physiology. Disruptions in potassium homeostasis, particularly hyperkalemia, have profound metabolic and clinical consequences. Maintaining potassium balance is therefore critical for both metabolic health and overall physiological function.


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## Conflict of interest

None.

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