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FUNDAMENTALS OF SYNERGISM IN CHEMISTRY

Igor Povar, Oxana Spinu, Natalia Bolocan

Moldova State University, Institute of Chemistry, 3 Academiei str., MD2028, ipovar@yahoo.ca, Republic of Moldova

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Introduction

Synergism in chemical systems is a fundamental phenomenon widely exploited across many scientific and technological fields, including catalysis, fluid dynamics, pharmaceuticals, and separation processes. Historically, the concept of synergism has been recognized in disciplines such as medicine, education, and physics, and has been a cornerstone of chemistry for nearly a century. In chemical contexts, synergism describes situations where the combined effect of two or more components surpasses the sum of their individual contributions. A classic example is solvent extraction, where the simultaneous use of two extractants improves the transfer of specific metal species from aqueous to organic phases beyond what either extractant can achieve alone. This enhancement often arises from the formation of mixed ligand complexes, which provide greater stability and solubility.

Such synergistic systems typically involve an acidic chelating agent paired with a neutral donor molecule. In charged complexes, counterions like cationic surfactants can facilitate complex formation, indicating that mixed complexes are not incidental but essential for synergism to emerge. Understanding the underlying mechanisms and characteristics of synergism is crucial for optimizing chemical processes and expanding their practical applications.

Results and Conclusions

Two main approaches exist for evaluating synergistic effects: experimental comparisons of individual components and their mixtures, and mathematical modeling to quantify interactions and predict system behavior. While experimentation offers direct observation, modeling provides deeper insight, especially in complex, multicomponent systems. This study identifies the formation of mixed complexes as a unifying principle governing various synergistic chemical processes. Although well documented in solvent extraction, this principle often remains unrecognized in broader chemical practice. Synergism arises from intricate molecular and ionic interactions influenced by the structure of reactants, kinetic and thermodynamic factors, and mechanistic pathways. For example, in acid-base mixtures distributed between aqueous and organic phases, enhanced buffering capacity results from mixed complex formation in the organic phase, emphasizing the importance of phase distribution and structural complementarity. The concept of synergism extends broadly, explaining improved efficiencies in metal extraction, enhanced solubilization of noble metals, advancements in surfactant-assisted systems, increased reactivity in bifunctional extractants, and cooperative effects in catalytic systems with multiple metal centers. It also sheds light on environmentally relevant chemical interactions and pharmaceutical drug behavior. Additionally, this work presents a thermodynamic framework based on a generalized reaction equation and standard thermodynamic data to predict synergism and antagonism in liquid-liquid extraction systems. The study defines a precise synergistic coefficient calculated from partial molar fractions, demonstrating that synergism is driven by the stability of mixed complexes. In contrast, antagonism originates from competitive reactions in the organic phase, such as ligand competition and unstable adduct formation. Strategies to optimize extractant ratios, modify chemical compositions, and control phase conditions (including pH and ionic strength) are proposed to maximize synergistic effects and minimize antagonism. This framework provides a valuable tool for designing advanced extraction systems and extends to other heterogeneous chemical processes. Mixed complex formation is a critical and often overlooked condition necessary for the manifestation of chemical synergism in heterogeneous multicomponent systems. Recognizing the role of these complexes enables more precise interpretation and control of synergistic and antagonistic effects in chemical processes. Mixed complexes, whether heteroligand, heterometallic, or both, act as key intermediates that can be engineered to achieve targeted functional outcomes. This conceptual framework opens new avenues for the rational design of multifunctional chemical systems. Synergistic mixtures can serve as cost-effective alternatives to single-function reagents, which frequently require extensive validation. Future research should prioritize early identification of mixed species during system design, employing integrated thermodynamic, kinetic, and theoretical characterization methods. This study is expected to open new perspectives in the development of "next-generation reagents", shifting the focus from costly individual reagents and complex regulatory processes toward synergistic mixtures. The importance of isolating and characterizing a wide range of mixed compounds prior to their application in subsequent reactions will also be emphasized, supported by detailed thermodynamic and kinetic knowledge derived from theoretical calculations. These results will significantly impact the rational design and targeted development of novel synergistic processes with tailored properties. Moving beyond empirical observations, such holistic approaches will deepen our understanding of chemical synergism and broaden its practical application across diverse fields, from analytical chemistry and pharmaceuticals to environmental technologies and hydrometallurgy.

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