Selenite-Induced Cataract as a Model for Cataract Diseases: Limitations, Considerations, and Alternative Approaches

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Abstract
Cataract diseases, characterized by the opacification of the lens, pose a significant global health burden. Animal models are invaluable for understanding cataractogenesis and testing potential treatments [1]. The selenite-induced cataract model has been widely used due to its rapid onset and predictable progression. However, this model has limitations that must be considered. This article reviews the limitations of the selenite-induced cataract model and explores alternative approaches that better represent the complexity and natural course of human cataract diseases [2].

Keywords: Animal models, Alternative approaches, Cataract, Selenite-induced cataract, Limitations

1. Introduction
Cataracts, the leading cause of visual impairment worldwide, necessitate effective research models for understanding their pathogenesis and developing therapeutic interventions. The selenite-induced cataract model has emerged as a popular choice due to its ability to induce lens opacification rapidly. However, despite its advantages, this model has certain limitations that need to be addressed to ensure the clinical relevance and translatability of findings.

2. Limitations of the Selenite-Induced Cataract Model
• Non-physiological Pathway
The selenite-induced cataract model primarily triggers cataract formation through oxidative stress-induced damage, whereas human cataracts are often multifactorial. Human cataracts involve complex interactions between genetic predisposition, age-related changes, and environmental factors such as ultraviolet radiation or long-term medication use [3]. Therefore, relying solely on the selenite-induced cataract model may oversimplify the diverse pathogenesis observed in human cataract diseases.

• Rapid Onset and Progression
The accelerated onset and progression of lens opacities in the selenite-induced cataract model enable efficient experimentation but fail to capture the gradual changes and long-term effects characteristic of age-related cataracts in humans [4]. Age-related cataracts develop slowly over time, making it crucial to consider alternative models that can mimic the progressive nature of the disease and allow for the evaluation of interventions at different stages [5].

• Lack of Lens Transparency
A significant limitation of the selenite-induced cataract model is the complete lens opacity induced by selenite in animal models [6]. This complete opacification impedes the observation and evaluation of specific stages or types of cataracts. Researchers often rely on gross observations rather than precise measurements of lens transparency, making it challenging to assess early cataract formation or evaluate the effectiveness of potential treatments targeted at specific stages [7].

• Variability in Response
The selenite-induced cataract model exhibits inter-individual variability in the response to selenite administration, resulting in inconsistent and unpredictable patterns of cataract development [8]. This variability poses challenges in experimental design, sample size determination, and data interpretation, potentially compromising the reproducibility and reliability of findings. Thus, alternative models that offer more consistent and predictable outcomes are desirable.
• Species-Specific Differences
The selenite-induced cataract model primarily utilizes rodent models such as rats and mice [9]. However, there are inherent differences between rodent and human lens physiology, structure, and susceptibility to cataracts. Humans have a more complex lens structure, different protein compositions, and distinct molecular pathways involved in cataract development [10]. Therefore, caution must be exercised when directly translating findings from rodent models to human cataract pathogenesis and potential treatments.

2.1 Alternative Approaches
To overcome the limitations of the selenite-induced cataract model and improve our understanding of cataract diseases, several alternative approaches have been explored:

• Genetic Models
Genetically modified animals, particularly mice with specific gene mutations associated with cataract formation, provide valuable insights into the genetic basis of cataracts. These models allow the study of specific cataract subtypes or genetic risk factors observed in humans, enabling a deeper understanding of disease mechanisms and potential therapeutic targets [11].

• Age-Related Models
Long-term studies in animal models that mimic the gradual age-related changes seen in human cataracts offer a more accurate representation of the natural course of age-related cataracts [12]. These models allow researchers to investigate the progressive nature of the disease, evaluate interventions at different stages, and assess the efficacy of potential therapies over time.

• In Vitro Models
In vitro models using lens epithelial cell cultures or human lens organoids provide controlled environments to study cellular and molecular mechanisms of cataractogenesis. These models offer the advantage of manipulating specific variables, investigating specific pathways, and conducting high-throughput screening of potential drugs or interventions. They also provide insights into the cellular and molecular changes associated with cataract development [13].

• Human Tissue Studies
Direct examination of human lens tissue obtained from cataract surgeries or postmortem samples provides a unique opportunity to study cataract pathogenesis in humans [14]. These studies allow for the examination of lens proteins, metabolic changes, and molecular pathways involved in cataract development. Human tissue studies provide invaluable data for understanding the disease at the molecular level and validating findings from animal models.

3. Conclusion
While the selenite-induced cataract model has contributed significantly to our understanding of cataractogenesis and potential therapeutic interventions, its limitations must be recognized. To enhance our understanding of cataract diseases, researchers should consider alternative approaches that better reflect the complexity, gradual progression, and etiology of human cataracts. Integrating multiple models, including genetic models, age-related models, in vitro systems, and human tissue studies, will facilitate a comprehensive understanding of cataract diseases and accelerate the development of effective treatments for patients.

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