

A NOVEL HYDROGEL-BRONCHIAL EPITHELIAL CELL SPHEROIDS FOR TOXICOLOGICAL EVALUATION

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Doi: <https://doi.org/10.34107/KSZV7781.10406>

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ABSTRACT

Respiratory diseases are the leading cause of death in the world according to reports from the Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO: third, chronic obstructive pulmonary disease; fourth, lower respiratory infections; and sixth, trachea, bronchus and lung cancers^[1]). These astounding statistics are attributed to certain risk factors that include but are not limited to air pollution and first to third-hand smoke. In addition, marijuana, the most commonly used illicit drug in the US, is becoming legal in certain states for recreational use. However, with the increase in use, the question of long-term respiratory health effects becomes crucial. In addition, evidence has emerged that US military personnel deployed to Iraq and Afghanistan may be at risk for developing respiratory symptoms and, in some cases, disabling chronic lung diseases including chronic bronchitis, emphysema, asthma, and constrictive bronchiolitis. Because of this public health concern, there seems to have a necessity for effective respiratory toxicology in vitro models. While still valuable, two-dimensional (2D) methods are simplistic and overlook important biological parameters that influence cellular behavior. The purpose of this study is to elucidate the efficacy of bronchial epithelial cells (Beas-2B) in a novel alginate-based spheroid as a three-dimensional (3D) cytotoxicity testing model. Toxicants including gun range dust and Δ^9 - tetrahydrocannabinol (Δ^9 THC) were used to verify if this model can be used for cytotoxicity testing. Viability of encapsulated Beas-2B cells was analyzed following exposure to gun range dust extract and Δ^9 - tetrahydrocannabinol THC. This study established that Beas-2B cells encapsulated in a novel alginate-chitin nanofiber hydrogel spheroid is an effective three-dimensional cytotoxicity testing model.

Keywords: Hydrogel, Spheroids, Alginate, Nanofiber, Respiratory Diseases, Bronchial Cells, Toxicology

INTRODUCTION

Respiratory diseases are the leading cause of death in the world according to reports from the Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO: third, chronic obstructive pulmonary disease; fourth, lower respiratory infections; and sixth, trachea, bronchus and lung cancers^[1]). The report states that respiratory diseases are preceded by heart disease and cancer respectively, however; lung cancer has been reported as the second most common type of cancer^[2]. Chronic obstructive pulmonary disease is a life-threatening lung disease that interferes with normal breathing and is far more than the clichéd “smokers cough.” More than 3 million people worldwide died from COPD in 2018, equal to 6% of deaths globally^[1]. In a 2013 report, deaths from chronic lower respiratory disease in the United States were on the brink of 150,000 deaths^[3]. Inflammatory respiratory diseases are amongst significant