EFFECTS OF SALBUTAMOL, PREDNISOLONE AND MONTELUKAST ON SERUM ELECTROLYTE, UREA AND CREATININE IN ASTHMA-INDUCED FEMALE SPRAGUE-DAWLEY RATS

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CERTIFICATION

This is to certify that this project work on **"EFFECTS OF SALBUTAMOL, PREDNISOLONE AND MONTELUKAST ON SERUM ELECTROLYTE, UREA AND CREATININE IN ASTHMA-INDUCED FEMALE SPRAGUE-DAWLEY RATS"** was carried out by **OSA-ISIBOR DIVINE EHINOMEN,** with matriculation number: **BMS2101669;** in partial fulfillment for the Award of Bachelor of Science (B.Sc) Degree in the Department of Physiology, School of Basic Medical Sciences, College of Medical Sciences, University of Benin, Benin City.

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DEDICATION

I sincerely dedicate this project work to God Almighty for His guidance, strength, and unfailing support. I also dedicate it to my beloved parents, **MR and MRS. OSA-ISIBOR**, in appreciation of their unwavering support, patience, and encouragement, which contributed greatly to the success of this project, and lastly to **MR. CHIDI EZE** for his support throughout my time at the **UNIVERSITY OF BENIN.**

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I am deeply grateful to my supervisor, **DR. O. E. O. ALOAMAKA,** for his invaluable guidance and support, throughout the preparation of this project.
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ABBREVATIONS

AERD: Aspirin-Exacerbated Respiratory Disease

$Al(OH)_3$) aluminium hydroxide

ANOVA: One-Way Analysis Of Variance

AAWI: Asthma Associated With Infection

BUN: Blood Urea Nitrogen

CBT: Cognitive-Behavioral Therapy

COPD: Chronic Obstructive Pulmonary Disease

$CysLT_1$:Cysteinyl Leukotriene Receptor Type 1

EIB: Exercise-Induced Bronchoconstriction

FEV_1: Forced Expiratory Volume In One Second (FEV_1)

HEPA Filters: High-Efficiency Particulate Air Filters

H&E: Haematoxylin and Eosin

IA: Infectious asthma

ICS: Inhaled Corticosteroids

IgE: Immunoglobulin E

IL-4: Interleukine-4

ILC2: Innate Lymphoid Cells

LMICs: Low and Middle Income Countries

LTRA: Leukotriene Receptor Antagonist

OVA: Ovalbumin

SEM: Standard Error Of The Mean

SABA: Short Acting B2-adrenegic Agonist

Th2: T-helper 2

VOCs: Volatile Organic Compounds

WHO: World Health Organization

ABSTRACT

Asthma is a chronic inflammatory disorder of the airways characterized by recurrent episodes of wheezing, coughing, breathlessness, and chest tightness. The aim of this study is to evaluate the effects of salbutamol, prednisolone, and montelukast on serum electrolyte, urea, and creatinine in asthma-induced female Sprague-Dawley rats. Methodology: Sixty-four (64) rats weighing 120-250 g were randomly assigned into eight groups (n = 8 per group): The negative control group (no asthma, untreated), positive control group (asthma-induced, untreated), and six treatment groups (groups 3-8) induced with asthma, receiving salbutamol (1 mg/kg), montelukast (10 mg/kg), prednisolone (3 mg/kg), Salbutamol/Prednisolone (1 mg/kg + 3 mg/kg), montelukast/prednisolone(10 mg/kg + 3mg/kg), Salbutamol/Montelukast (1 mg/kg + 10 mg/kg). Groups 2-8 were sensitized via intraperitoneal injections of 1 mg ovalbumin (OVA), emulsified in 20 mg aluminum hydroxide (in 0.9% saline) on days 1 and 7 of the third week. From day 21, sensitized rats were challenged by exposure to aerosolized 1% OVA solution for 15 minutes per session, twice weekly for 28 days. Treatment continued throughout the challenge period. At the end of the treatment period, animals were anesthetized, and blood was collected for biochemical analysis. All data were expressed as mean ± Standard Error of Mean (SEM) and analyzed with one-way analysis of variance (ANOVA), followed by Tukey's post hoc test, using Graphpad Prism 10.2.2 software. Results showed a statistically significant increase in serum urea and creatinine in the prednisolone/montelukast-treated group compared with negative control ($p<0.05$), whereas prednisolone alone significantly decreased serum creatinine and potassium levels ($p<0.05$). No significant changes in serum urea, creatinine, potassium, sodium or chloride were observed in the salbutamol, montelukast, and their combination groups compared with the negative control ($p>0.05$). Compared with the positive control, several treatments, including montelukast, prednisolone, salbutamol/montelukast, and prednisolone/montelukast, significantly decreased serum urea, while prednisolone/montelukast, also increased sodium and decreased chloride levels ($p<0.05$). These findings suggest that prednisolone, particularly in combination with montelukast, can modulate renal function and eletrolyte balance, whereas salbutamol and montelukast alone exert minimal effects on kidney parameters.

CHAPTER 1
INTRODUCTION

1.1 BACKGROUND OF STUDY

Asthma is a chronic inflammatory disease of the airways that leads to episodic airflow obstruction, bronchial hyperactivity with the inflammatory component being pivotal to the pathogenesis of symptoms (Mandlik, 2020), which include wheezing, coughing, shortness of breath, chest tightness, fatigue and increased mucus production (NHDI, 2022). Some of the stimuli or triggers of asthma attacks include viral upper respiratory infections, pollen, dust mites, molds, animal danger, occupational chemicals, tobacco smoke, cold air, exercise, sinus infections, emotional factors, and drugs such as aspirin (Wenzel, 2012). A trigger (smoke, mold) initiates the airway inflammatory response in asthma (Galli *et al.,* 2008). After inhalation, these triggers may stimulate resident airway mast cells and cause cross-linking of immunoglobulin E on the mast cell surface (Galli *et al.,* 2008). This will result in the release of histamine and will induce the production of prostaglandins, leukotrienes (Galli *et al.,* 2008). Simultaneously, cytokines derived from the mast cell will signal other inflammatory cells and their mediators to the lung (Barnes, 2008). The result is airway inflammation, increased vascular permeabiity, mucus secretion, bronchospasm, and wheezing, these events are referred to as the early asthmatic response because they occur within minutes (Holgate, 2012). The late asthmatic response is delayed by hours. It is caused by a multitude of inflammatory cells continuing the inflammatory process (Wenzel, 2012). Of the inflammatory cells, the T cells play an important role (Barnes, 2008). Antigen presenting cells may present a variety of allergenic antigens to chronically activated T helper cells (Barnes, 2008). These cells then secrete multiple cytokines that maintain and intensify the local inflammatory response (Barnes, 2008). Many other inflammatory cells, including mast cells and eosinophils, will respond to the T cells cytokines (Barnes, 2008). These inflammatory cells will produce cytokines, which amplify the cellular response and the inflammatory reaction (Galli *et al.,* 2008).

Asthma management focuses on symptom control and preventing exacerbation (GINA, 2023). It includes, taking medications such as, Leukotriene receptor antagonist(LTRA), (e.g., montelukast, pranlucast), that blocks Cysteinyl Leukotriene Receptor Type 1. (CysLT1) receptors, preventing leukotriene-induced bronchoconstriction, inflammation and mucus production in asthma (GINA, 2023).

LTRAs are used for long-term asthma control and allergic rhinitis. Also taking short-acting beta-agonist like, Salbutamol, a short acting B2-adrenegic agonist (SABA), is used for quick relief of asthma symptoms (Thomson *et al.*, 2013). It relaxes bronchial smooth muscle by stimulating B2-receptors, leading to bronchodilation and improved airflow reducing wheezing, shortness of breath and chest tightness in asthma patients (Barnes, 2018). Another vital asthma medication is Prednisolone which a systemic corticosteroid with potent anti-inflammatory properties (Lipworth, 2014). It also reduces eosinophil recruitment and vascular permeability, as a result, airway inflammation is rapidly controlled during exacerbations (Reddel *et al.*, 2015).

Research indicates that asthma can significantly affect serum electrolyte, urea, and creatinine levels. Serum electrolyte disturbances can arise due to hyperventilation or acid-base imbalances (Ali *et al*., 2019). Potassium plays a vital role in neuromuscular transmission and smooth muscle function (Palmer, 2015). Hypokalemia (low potassium levels) is commonly observed in asthma patients using β_2-agonists, such as salbutamol (Lipworth, 2018). These medications stimulate Na^+/K^+ ATPase, causing intracellular potassium shifts and reducing serum potassium levels (Lipworth, 2018). Magnesium is essential for bronchodilation and neuromuscular stability. Also, Hypomagnesemia has been associated with increased airway hyper-responsiveness and a higher risk of asthma exacerbations (Yeh *et al*., 2016). Sodium is involved in fluid balance and acid-base homeostasis (GINA, 2023). Urea also, is a byproduct of protein metabolism excreted by the kidneys (Hanada *et al.*, 2019). Elevated blood urea nitrogen (BUN) levels in asthma patients may indicate dehydration, hypoxia-induced kidney dysfunction, or corticosteroid-induced catabolism (Leung *et al*., 2021). Severe asthma attacks can lead to increased respiratory rate and insensible water loss, causing dehydration and increased urea concentration in the blood (Hanada *et al.,* 2019). Prednisolone leads to sodium retention and potassium loss, contributing to hypertension and hypokalemia (Morris, 2013). Long-term corticosteroid therapy can enhance protein breakdown, increasing urea production (Lipworth, 2018). Montelukast, has minimal impact on electrolyte balance (Grobost*,* 2015). It is also generally well-tolerated in the kidneys, but some studies report mild elevations in serum urea and creatinine, possibly due to hypersensitivity reactions or renal involvement in systemic inflammation (Ramesh, 2017). Creatinine is a metabolic waste product derived from muscle metabolism and serves as a key indicator of kidney function (NIDDK, 2018). Its levels in blood and urine can be influenced by

asthma-related factors such as hypoxia, dehydration, and medication effects (NIDDK, 2018). Severe asthma with prolonged hypoxia may reduce renal blood flow, leading to impaired creatinine clearance and an increase in serum creatinine levels (Singh *et al.,* 2020).

Ovalbumin (OVA) is widely used to create allergic asthma models in Sprague-Dawley rats, mimicking human asthma pathology, this helps in the understanding of asthma symptoms and triggers so as to administer proper drugs and management plans to asthma patients (González-González, 2020). The histological changes in lung tissues of rat models include, increased goblet cell proliferation within the bronchial epithelium, leading to excessive mucus secretion, which then contributes to airway obstruction (Chu *et al*., 2021), increased vascular permeability results in interstitial edema and vascular congestion, worsening airway inflammation (Yiamouyiannis *et al*., 2018).

1.2 JUSTIFICATION OF STUDY

Asthma is a widespread chronic disease that requires continuous medication for effective management. While drugs like salbutamol, prednisolone, and montelukast are commonly used, their potential effects on serum electrolyte balance and metabolic waste markers such as urea and creatinine are not fully understood. Existing evidence suggests that these medications may alter serum levels, potentially leading to complications if not properly monitored. Understanding these effects is important for improving treatment strategies and ensuring patient safety. This research will help bridge the knowledge gap regarding the systemic impacts of asthma medications.

1.3 AIM OF STUDY

To evaluate how salbutamol, prednisolone, and montelukast affect serum electrolyte, urea, and creatinine in asthma-induced Sprague-Dawley rats.

1.4 STATEMENT OF PROBLEM

Asthma is a chronic inflammatory airway disease that can alter serum electrolyte, urea, and creatinine levels through disease mechanisms and medication effects. However, limited research exists on how common asthma treatments, such as salbutamol, prednisolone, and montelukast affect these biomarkers, particularly in Sprague

Dawley rats. This gap hinders a complete understanding of their systemic impact, which is crucial for optimizing asthma management.

1.5 RESEARCH QUESTIONS

1. What are the effects of salbutamol, prednisolone and montelukast on serum electrolyte, urea and creatinine in asthma-induced female Sprague-Dawley rats?
2. What are the effects of the combinations of these asthma medications on serum electrolyte, urea and creatinine in asthma-induced female Sprague-Dawley rats?

1.6 SPECIFIC OBJECTIVE

To assess changes in serum electrolyte, urea, and creatinine levels following administration of salbutamol, prednisolone, and montelukast in asthma-induced female Sprague-Dawley rats.

CHAPTER TWO
LITERATURE REVEIW

2.1 EPIDEMIOLOGY OF ASTHMA

As of 2022, approximately 300 million people worldwide were affected by asthma, and about 400,000 people die from asthma each year worldwide (Global Asthma Report, 2022). Most of these deaths occur in low and middle income countries, where access to effective treatment and asthma management is limited (Global Asthma Report, 2022; WHO, 2023). Low and middle income countries (LMICs) account for approximately over 90% of global asthma-related deaths each year (WHO, 2023; Global Asthma Report, 2022). Prevalences vary between countries from 1% to 18% (Global Initiative for Asthma, 2011).

Asthma tends to be more prevalent in developed than in developing countries (Global Initiative for Asthma, 2011). Rates are lower in Asia, Europe, and Africa (Mason *et al.*, 2010). In Asia, prevalence varies widely, low in rural areas, higher in urban centers (Global Initiative for Asthma, 2011). In China and India, prevalence is estimated between 2% and 11%, depending on age and location (Global Initiative for Asthma, 2011). While Europe, asthma is common, especially in Western and Northern Europe. The UK reports some of the highest rates, around 8–12% of the population (European Lung Foundation, 2022). Asthma prevalence is rising in Africa, especially in urban areas. Estimates range from 5% to 20% in children in some countries. The lack of diagnosis and poor access to treatment affect accurate reporting (Ait-Khaled *et al.,* 2012). The burden of asthma is of public health concern because asthma is a major cause of infirmity, depletes scarce health resources, and reduces the quality of life of affected individuals (Onoka *et al*.,2010). This burden is even more profound in developing countries like Nigeria, where health costs are largely borne by the individual patient (Onoka *et al*.,2010). Overall, the estimated national clinical prevalence of asthma in Nigeria is around 6.4%, though localized studies suggest rates up to 15% in certain communities or age groups (Desalu *et al.*, 2019; Global Asthma Network, 2022). In other African countries like South Africa, the prevalence of asthma is significantly high, particularly among adolescents (Global Asthma Network, 2022). Data from Cape Town indicate that approximately 21.3% of adolescents aged 13–14 years reported current wheezing symptoms, while 16.6% reported having ever been diagnosed with asthma (Global Asthma Network, 2022). Among adults, nationally representative data estimate a clinical asthma prevalence of 6.1%, with

12.4% experiencing wheezing symptoms within the previous 12 months (Braman, 2012). Asthma prevalence is high in North America, it affects approximately 8% of the population of the United States and causes approximately 4,210 deaths per year (Lazarus, 2010; Centers for Disease Control and Prevention, 2023). While in South America, asthma demonstrates a moderate to high prevalence, with epidemiological data indicating that 10–20% of children are affected, particularly in countries such as Brazil and Argentina (International Study of Asthma and Allergies in Childhood, 2013). Also, Australia reports one of the highest asthma prevalence rates globally, with approximately 11% of the population affected by the condition (Australian Institute of Health and Welfare, 2023).

2.1.1 Classes of Asthma

Asthma can be classified clinically based on symptom frequency, spirometric parameters such as forced expiratory volume in one second (FEV_1), and peak expiratory flow rate (Yawn, 2018). Broadly, asthma is divided into atopic (extrinsic) and non-atopic (intrinsic) types, depending on whether allergic triggers are present (Kumar *et al.*, 2010). While traditional classifications emphasize severity and control, modern research is increasingly focused on identifying treatable traits and immunological endotypes, particularly distinctions between type 2 and non-type 2 inflammation (Harrison, 2022). This evolving classification system facilitates precision medicine, enabling personalized therapies (Moore *et al.*, 2010).

Acute Severe Asthma

Formerly termed *status asthmaticus*, this is a life-threatening exacerbation unresponsive to standard therapies such as bronchodilators and corticosteroids (Shah *et al.,* 2012). It is commonly triggered by infections, allergens, pollution, or inadequate medication use (Shah *et al.,* 2012).

Brittle Asthma

This rare but severe phenotype is marked by recurrent, unpredictable attacks (British Guideline on the Management of Asthma, 2009). Type 1 presents with wide variability in peak expiratory flow despite optimal treatment, whereas Type 2 is characterized by sudden, severe attacks in otherwise controlled asthma (British Guideline on the Management of Asthma, 2009).

Exercise-Induced Bronchoconstriction (EIB)

Physical activity induces bronchoconstriction in most asthmatics and up to 20% of non-asthmatics (Khan, 2012). It is prevalent among elite athletes, especially cyclists, swimmers, and skiers, often worsening in cold, dry air (Wuestenfeld *et al*., 2010; GINA, 2011).

Occupational Asthma

This variant arises from workplace exposures and accounts for 5-25% of adult asthma cases (Baur *et al.*, 2012). High-risk occupations include spray painters, bakers, hairdressers, welders, and healthcare workers exposed to allergens such as isocyanates, dust, and latex (Kunnano, 2005).

Aspirin-Exacerbated Respiratory Disease (AERD)

Also known as aspirin-induced asthma, AERD includes asthma and chronic rhinosinusitis with nasal polyps (Kennedy, 2016). It affects up to 9% of asthmatics and may present with alcohol-induced respiratory symptoms (Chang, 2012; Kennedy, 2016).

Alcohol-Induced Asthma

Alcohol exacerbates asthma symptoms in approximately one-third of patients, with higher prevalence reported in individuals of East Asian descent and those with AERD (Adams *et al.*, 2013). Interestingly, some patients report symptom relief from alcohol (Adams *et al.*, 2013).

Non-Atopic (Intrinsic) Asthma

Comprising 10-33% of cases, non-atopic asthma often presents later in life and is more common in women (Peters, 2014). Despite negative skin tests for allergens, elevated serum immunoglobulin E (IgE) levels suggest an allergic basis may still exist (Burrows, 1989; Hahn, 2021).

Infectious Asthma

This subtype often follows a respiratory infection that precipitates asthma (Hahn *et al.,* 2022). Termed infectious asthma (IA) or asthma associated with infection (AAWI), it is under-recognized in clinical practice despite evidence suggesting it accounts for up

to 70% of severe adult-onset cases (Hahn *et al.,* 2022; Rantala, 2011). A Finnish study found 35.8% of new-onset asthma cases had experienced lower respiratory infections within a year prior to onset (odds ratio: 7.2) (Rantala, 2011).

2.1.2 PATHOPHYSIOLOGY OF ASTHMA

Asthma is a chronic inflammatory disease of the airways marked by reversible airflow obstruction, bronchial hyperresponsiveness, and airway inflammation (Papi *et al*., 2018). The pathogenesis involves a dynamic interaction of immunological mechanisms, structural airway alterations, and environmental stimuli, culminating in the clinical symptoms of wheeze, dyspnea, chest tightness, and cough (Barnes, 2011).

The disease process is initiated by activation of immune cells such as mast cells, eosinophils, T-helper 2 (Th2) lymphocytes, macrophages, and, in certain phenotypes, neutrophils (Holgate, 2012). Upon allergen or irritant exposure, these cells release pro-inflammatory cytokines including interleukins IL-4, IL-5, and IL-13 (Lambrecht *et al.*, 2015). IL-4 promotes class switching to IgE production in B cells, IL-5 facilitates eosinophil recruitment and longevity, IL-13 contributes to mucus metaplasia and airway hyperresponsiveness, (Lambrecht *et al.*, 2015).

Allergic asthma involves IgE-mediated sensitization, where allergen-specific IgE binds to high-affinity FcεRI receptors on mast cells (Galli *et al.*, 2008). Upon subsequent allergen exposure, cross-linking of IgE triggers mast cell degranulation, releasing histamine, leukotrienes, and prostaglandins that induce acute bronchoconstriction, increased vascular permeability, and mucus secretion, forming the early-phase reaction (Gould *et al.*, 2008; Galli *et al.,* 2008).

A late-phase reaction follows several hours later, characterized by further inflammatory cell recruitment, especially eosinophils (Kraft *et al.*, 2020). These cells release toxic granules, including major basic protein and eosinophil peroxidase, which damage the airway epithelium and sustain inflammation, contributing to persistent symptoms and airway remodeling (Bousquet *et al*., 2000; Kraft *et al.*, 2020).

Airway hyperresponsiveness, a core feature of asthma, reflects an exaggerated bronchoconstrictive response to a variety of stimuli such as allergens, cold air, or exercise (Cockcroft *et al.*, 2006. This hyperreactivity arises from inflammatory mediator-induced smooth muscle sensitization and structural airway changes such as wall thickening and fibrosis (Cockcroft *et al*., 2006; Pavord *et al*., 2018).

Chronic inflammation induces airway remodeling, encompassing subepithelial fibrosis via collagen deposition, goblet cell hyperplasia, smooth muscle hypertrophy, increased angiogenesis, and basement membrane thickening (Bergeron *et al.*, 2009). These changes can result in irreversible airflow limitation and reduced bronchodilator responsiveness (Holgate, 2012; Bergeron *et al.*, 2009).

Mucus hypersecretion is a pathological hallmark, driven by goblet cell hyperplasia and mucin gene overexpression (notably MUC5AC) leading to the formation of tenacious mucus plugs that contribute to airflow obstruction and hypoxemia, particularly during exacerbations (Fahy *et al*., 2010).

Non-allergic and severe asthma phenotypes often exhibit neutrophil-dominant inflammation, reduced steroid responsiveness, and involvement of Th17 and innate lymphoid cells (ILC2), with key cytokines such as IL-17 contributing to pathogenesis (Rays *et al*., 2017). These phenotypes are frequently associated with more persistent, refractory forms of the disease (Wenzel, 2012).

2.2 ASTHMA MANAGEMENT AND MEDICATION OVERVIEW

Managing asthma requires a combination of bronchodilators, anti-inflammatory agents, and, in some cases, leukotriene modifiers (Bateman *et al.*, 2008). Three widely used drugs which include salbutamol, prednisolone, and montelukast are central to this treatment strategy (Reddel *et al.,* 2015).

2.3 Salbutamol

Salbutamol, introduced in 1968, was the first clinically available selective short-acting β2-adrenergic receptor agonist (SABA) and has since become a cornerstone in the management of acute bronchospasm associated with asthma and other chronic obstructive pulmonary conditions (Makhlouf *et al.*, 2002). As a β2-selective agonist, salbutamol acts primarily on airway smooth muscle to induce bronchodilation, thereby providing rapid relief from acute respiratory symptoms (DrugBank, 2022). Its efficacy in relieving and preventing bronchospasm underpins its widespread clinical use and its inclusion on the World Health Organization's Model List of Essential Medicines, signifying its critical role in global healthcare delivery (WHO, 2021).

Salbutamol is typically recommended for symptom relief rather than as monotherapy, and current guidelines advocate for its use in conjunction with inhaled corticosteroids (e.g, beclomethasone), particularly to mitigate the risk of exacerbations associated

with over-reliance on bronchodilators alone (Gauvreau *et al*., 1997). Notably, frequent or regular use of salbutamol may paradoxically lead to a subtle decline in asthma control over time (Taylor *et al.*, 1991; Ullmann *et al.*, 2015). Emerging evidence suggests that chronic exposure to β2-agonists may exert pro-inflammatory effects by increasing the expression of inflammatory mediators, potentially exacerbating airway hyperresponsiveness and obstruction (Gauvreau *et al.*, 1997; Ritchie *et al.,* 2018). This raises important concerns regarding the long-term safety of β2-agonist overuse, reinforcing the need for balanced and guided therapeutic strategies in asthma management (Global Initiative for Asthma, 2023).

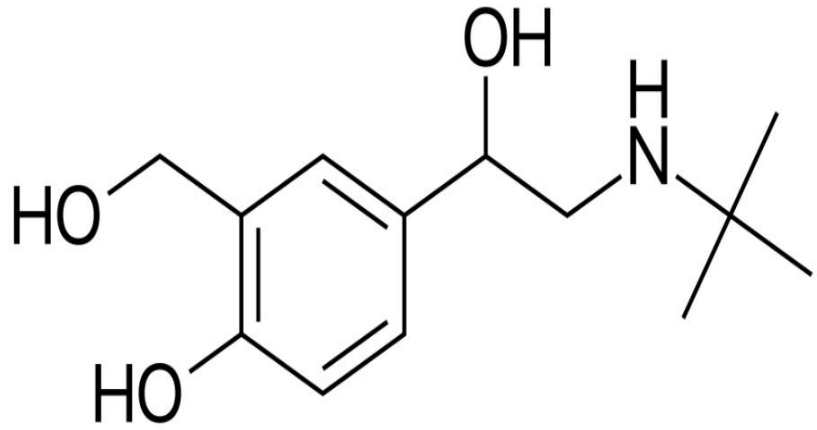

Figure 1: Chemical Structure Of Salbutamol

Source: Kaul Hoffmeier, (2007).

2.3.1 Mechanism Of Action

The smooth muscle of the respiratory tract is constituted by a large number of β_2-receptors (Emeryk *et al*., 2021). Their activity is mediated by the production of cyclic adenosine monophosphate (AMP) as a second messenger (Kim *et al.*, 2021). Therefore, as an agonist, salbutamol binds reversibly to these receptors, which are believed to be adenyl cyclase, resulting in the conversion of cyclic AMP (Emeryk *et al*., 2021). Cyclic AMP then triggers a cascade of intracellular events that culminate in the inhibition of the contraction of bronchial smooth muscle, thereby promoting smooth muscle relaxation and bronchodilation, its therapeutic effect (Emeryk *et al*., 2021). Salbutamol also inhibits the release of immediate hypersensitivity mediators from cells, particularly mast cells (Price *et al.*, 1989). Due to its high selectivity, salbutamol has minimal activity on β_1-adrenergic receptors (Price *et al.*, 1989).

2.3.2 Effects Of Salbutamol On Serum Electrolyte, Urea And Creatinine

Salbutamol, a short-acting β2-adrenergic receptor agonist (SABA), is widely used for the rapid relief of bronchospasm due to its potent bronchodilatory effects mediated through relaxation of airway smooth muscle (Lipworth, 2018). Despite its therapeutic efficacy, systemic administration or high-dose inhalation of salbutamol has been associated with several metabolic derangements, notably disturbances in electrolyte homeostasis (Lipworth, 2018). A key mechanism involves the stimulation of the sodium-potassium ATPase pump, which facilitates intracellular translocation of potassium, thereby predisposing patients to hypokalemia, a condition that may manifest clinically as muscle weakness, cardiac arrhythmias, and in some instances, worsening asthma symptoms (Palmer, 2015).

Moreover, salbutamol has been implicated in the enhancement of renal magnesium excretion, leading to hypomagnesemia, a phenomenon particularly relevant during intensive β2-agonist therapy for acute asthma exacerbations (Cheung *et al.*, 2015). These alterations in electrolyte levels underscore the importance of careful monitoring, especially in patients receiving repeated or high doses (Ullmann *et al.,* 2010). Although less frequently reported, deviations in serum urea and creatinine concentrations have also been observed, particularly in cases of dehydration or excessive β2-agonist use, highlighting a potential renal impact under certain clinical circumstances (Ullmann *et al.*, 2010).

2.4 Prednisolone

Prednisolone is a type of systemic corticosteroid that is commonly used to treat inflammation in various conditions, including asthma, chronic obstructive pulmonary disease (COPD), and autoimmune diseases (Lipworth, 2014; Barnes, 2011). It works by reducing inflammation and suppressing the immune response (Bateman *et al*., 2008). In asthma, it helps control symptoms during severe attacks by decreasing the production of substances that cause inflammation, such as cytokines and chemokines (Bateman *et al*., 2008).

Prednisolone is the active form of prednisone, which is a prodrug that must be converted by the liver into prednisolone before it becomes effective (Buttgereit, 2013). Once active, it binds to glucocorticoid receptors inside cells, stopping the production of inflammatory molecules (Holgate, 2012). It also lowers the number of eosinophils (a type of immune cell involved in asthma) and reduces the leakage of fluid into the

airways, which helps open them up and improve breathing (Global Initiative for Asthma, 2023; Reddel *et al.*, 2015).

The drug is usually taken by mouth and is often used for a short period during asthma exacerbations (Lipworth, 2014). However, long-term use can lead to side effects such as weight gain, high blood pressure, bone thinning (osteoporosis), high blood sugar, muscle weakness, mood changes, and a higher risk of infections (Barnes, 2011; Holgate, 2012; British National Formulary, 2018). It can also cause skin problems like easy bruising and oral infections like thrush (British National Formulary, 2018). Because of these risks, doctors try to limit how long patients take it, and tapering the dose is important to avoid withdrawal problems (British National Formulary, 2018).

Prednisone was developed in the 1950s and is now widely used around the world. It is listed on the World Health Organization's (WHO) list of essential medicines because of its importance in treating serious illnesses (WHO, 2023). It is also available in generic form and was one of the most commonly prescribed medications in the United States in 2022, with over 18 million prescriptions filled (Clincalc, 2024).

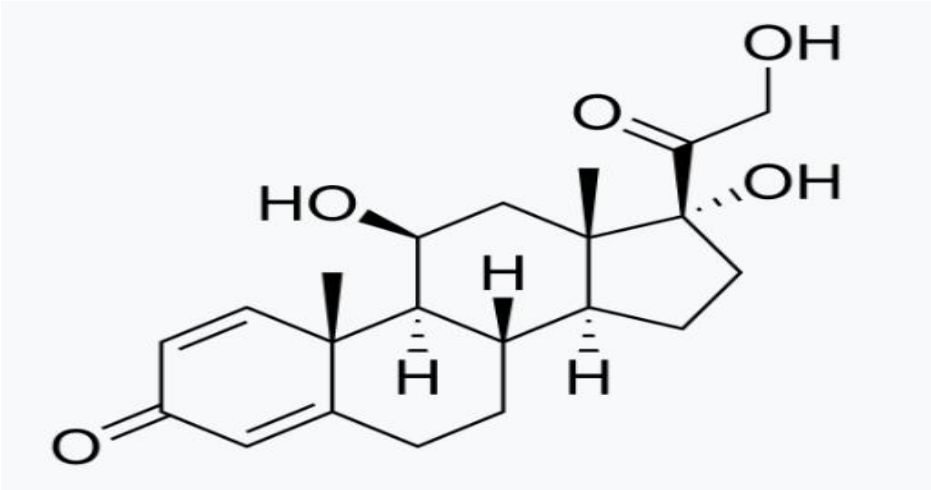

Figure 2: Chemical Structure Of Prednisolone

Source: PubChem, (2023).

2.4.1 Mechanism Of Action

Steroids like prednisone reduce inflammation by inhibiting phospholipase A2 (PLA2), an enzyme that releases arachidonic acid from cell membrane (Wang *et al.*, 2021). This prevents the production of pro-inflammatory mediators like prostaglandins and leukotrienes (Wang *et al.*, 2021). Prednisone reduces inflammation by suppressing the migration of polymorphonuclear leukocytes and reversing increased capillary

permeability (Wang *et al.*, 2021). Prednisone also suppresses the immune system by decreasing the activity and volume of the immune system (Wang *et al.*, 2021). The antineoplastic effects may correlate with inhibiting glucose transport, phosphorylation, or induction of cell death in immature lymphocytes (Wang *et al.*, 2021). Prednisone may also demonstrate anti-emetic effects (the ability of a substance or drug to prevent or reduce nausea and vomiting), by blocking the emetic center's cerebral innervation via prostaglandin inhibition (Wang *et al.*, 2021).

Prednisone is a prodrug to prednisolone, which mediates its glucocorticoid effects (Cai *et al.*, 2025). After cell surface receptor attachment and entry into the cell, prednisone enters the nucleus, binds, and activates specific nuclear receptors, resulting in altered gene expression and inhibiting pro-inflammatory cytokine production (Stortz *et al*., 2019). This agent decreases the number of circulating lymphocytes, inducing cell differentiation, and stimulates apoptosis in sensitive tumor cell populations (Stortz *et al*., 2019). The effects of glucocorticoids are subject to mediation by mechanisms that alter DNA replication within the nucleus (Stortz *et al*., 2019).

2.4.2 Effects Of Prednisolone On Serum Electrolyte, Urea And Creatinine

Prednisolone is a systemic corticosteroid used in asthma for its potent anti-inflammatory effects (Morris 2013). While beneficial for controlling airway inflammation, long-term or high-dose corticosteroid use can cause significant metabolic and renal effects (Morris 2013). Prednisolone contributes to sodium retention and potassium excretion by acting on mineralocorticoid receptors, often leading to hypernatremia (a condition characterized by elevated sodium levels in the blood), and hypokalemia (a medical condition characterized by low levels of potassium (K^+) in the blood),(Morris, 2013; Adrogue *et al.*, 2000; Gennari, 1998). These imbalances can increase the risk of hypertension and cardiac complications (Morris, 2013).

Furthermore, prednisolone increases protein catabolism, leading to elevated levels of nitrogenous waste products such as urea in the blood (Leung *et al.*, 2021). This elevation may mimic renal impairment in biochemical tests, especially during prolonged therapy (Leung *et al.,* 2021). It may also slightly elevate serum creatinine levels by reducing renal perfusion or through increased muscle breakdown (Singh *et al.*, 2020). Additionally, prednisolone can contribute to glucocorticoid-induced

osteoporosis and muscle wasting, both of which indirectly affect metabolic markers such as creatinine (Van Staa *et al.*, 2002).

2.5 Montelukast

Montelukast, sold under the brand name Singulair among others, is a medication used in the maintenance treatment of asthma (Anon, 2000). Montelukast is a leukotriene receptor antagonist (LTRA). It blocks the cysteinyl leukotriene receptor (CysLT1) in airway tissues (Barnes, 2011). Leukotrienes are inflammatory mediators released by mast cells and eosinophils (Holgate, 2012). They cause bronchoconstriction, mucus secretion and vascular leakage (GINA, 2023). By blocking leukotriene action, montelukast reduces inflammation and bronchospasm (Bateman *et al.*, 2008). It is used in mild to moderate asthma and allergic rhinitis (Reddel *et al.,* 2015). Montelukast is especially useful in exercise-induced and aspirin-sensitive asthma (Wenzel, 2012). Although less effective than inhaled corticosteroids (e.g, beclomethasone), it improves symptom control (Barnes, 2011). Montelukast is taken orally and is well-tolerated in children (Holgate, 2012). Common side effects include abdoninal pain, cough, and headache (Anon, 2000). Severe side effects may include allergic reactions, such as anaphylaxix and eosinophilia (Anon, 2000). Use in pregnancy appears to be safe.

Montelukast was approved for medical use in the United States in 1998 (Anon, 20000. It is available as a generic medication. In 2022, it was the seventeenth most commonly prescribed medication in the United States, with more than 29 million prescriptions (ClinClac, 2024).

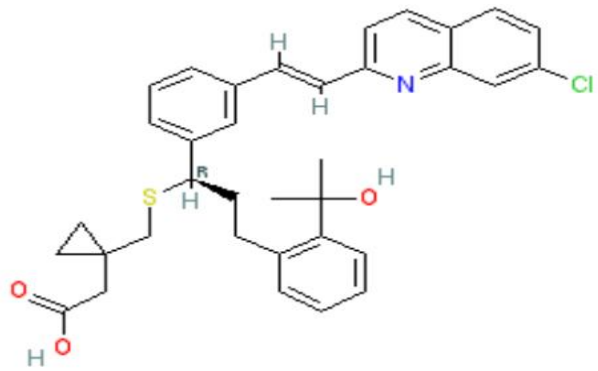

Figure 3: Chemical Structure Of Montelukast

Source: DrugBank, 2024.

2.5.1 Mechanism Of Action

Montelukast is a highly selective leukotriene receptor antagonist that binds with high affinity to the cysteinyl leukotriene receptor for leukotrienes D4 and E4 (Castro-Rodriguez *et al*., 2018). These leukotrienes are excreted by various cells, such as mast cells, and are involved in the inflammatory process that may cause asthma and signs and symptoms (Castro-Rodriguez *et al*., 2018). Leukotriene receptors are found in airway cells, such as macrophages and smooth muscle cells (Castro-Rodriguez *et al*., 2018). When bound to leukotriene receptors, montelukast inhibits leukotriene physiologic effects (such as airway edema, smooth muscle contraction, and impairment of normal cellular activity) without exhibiting any agonist activity (Castro-Rodriguez *et al*., 2018). In asthmatics, low doses of montelukast (5 mg) induce a significant inhibition of bronchoconstriction caused by leukotriene D4 (Castro-Rodriguez *et al*., 2018). Furthermore, in a crossover study, montelukast inhibited early and late-phase bronchoconstriction caused by a challenge with antigen in 12 asthmatic patients (Castro-Rodriguez *et al*., 2018). Most international asthma guidelines advise that children ≤5 years old with asthma be treated with daily low-moderate dose inhaled corticosteroids (ICS) as the preferred controller and montelukast as an alternative therapy (Castro-Rodriguez *et al*., 2018).

2.5.2 Effects Of Montelukast On Serum Electrolyte, Urea And Creatinine

Unlike corticosteroids or β2-agonists, montelukast is generally well tolerated and has minimal systemic side effects (Ramesh *et al.*, 2017).

However, a few studies suggest that montelukast may cause mild elevations in serum urea and creatinine, potentially linked to hypersensitivity reactions or rare nephrotoxic effects (Ramesh *et al.,* 2017).

Montelukast has negligible effects on electrolyte balance (Grobost, 2015). There are no consistent reports of montelukast altering serum potassium, sodium, or magnesium levels in blood under normal therapeutic conditions (Grobost, 2015). Nonetheless, it is prudent to monitor renal function when prescribing montelukast in patients with pre-existing renal impairments or systemic inflammatory conditions (Ramesh *et al*., 2017)

2.6 Combined Effects Of Salbutamol, Prednisolone And Montelukast On Serum Electrolyte, Urea And Creatinine

The simultaneous use of these medications in asthma treatment may have additive or synergistic effects on renal and electrolyte parameters (Lipworth, 2018). For instance, a patient on both prednisolone and salbutamol is at increased risk of hypokalemia, which requires routine serum potassium monitoring (Morris, 2013). Additionally, cumulative effects on renal function must be considered in long-term therapy or in patients with underlying kidney disease (Leung *et al*., 2021).

Furthermore, in experimental settings and animal models such as Sprague Dawley rats exposed to asthma inducers like ovalbumin (OVA), treatment with these drugs may lead to measurable alterations in biochemical markers (González-González, 2020). Such studies often reveal that salbutamol and prednisolone, due to their systemic activity, more profoundly impact electrolyte and nitrogenous waste excretion than montelukast (Ramesh *et al.*, 2017). These findings highlight the importance of biochemical monitoring in both clinical and research contexts (Hanada *et al.,* 2019).

2.7 NON-MEDICATIONAL ASTHMA MANAGEMENT

Patient Education and Self-Management

Patient education is one of the most effective tools for asthma management (Pinnock *et al.,* 2017). It involves educating patients about asthma pathophysiology, medication use, early recognition of exacerbations, and appropriate response to symptoms (Pinnock *et al.,* 2017). Personalized asthma action plans, developed collaboratively between healthcare providers and patients, improve adherence to treatment and reduce emergency visits (Ahmed *et al.*, 2022). These plans outline step-by-step instructions for daily management and how to handle worsening symptoms (Ahmed *et al.,* 2022)

Trigger Avoidance

Avoiding exposure to known asthma triggers significantly helps in preventing symptoms (Global Initiative for Asthma. 2023). Common triggers include, allegens (dust mites, pet dander, mold), tobacco smoke, air pollution, cold air, strong odors, and respiratory infections (Bousquet *et al.,* 2010). Environmental control measures such as using allergen-proof bedding, vacuuming with HEPA filters (high-efficiency particulate air filters, are advanced air filtration systems designed to trap a high percentage of very small airborne particles, reducing indoor humidity), and avoiding

secondhand smoke have demonstrated effectiveness in sensitive individuals (Arroyave *et al.,* 2021; Sublett *et al*., 2010).

Pulmonary Rehabilitation and Breathing Techniques

Pulmonary rehabilitation, including supervised exercise training, breathing retraining, and physical activity promotion, has shown benefits in improving respiratory muscle strength and exercise tolerance (McGillivray *et al.,* 2019). Breathing techniques like the Buteyko method and diaphragmatic breathing may help reduce hyperventilation and improve symptom perception, although their effectiveness varies (Holloway *et al.,* 2020).

Psychological Support

Asthma has been associated with higher levels of anxiety and depression, which can worsen symptom perception and reduce adherence to therapy (Yorke *et al*., 2013). Cognitive-behavioral therapy (CBT) and mindfulness-based interventions have been shown to improve asthma-related quality of life and psychological outcomes (Thomas *et al.*, 2015). Addressing mental health is therefore an essential component of holistic asthma care (Thomas *et al*., 2015).

Weight Management and Nutrition

Obesity is a recognized risk factor for asthma incidence and severity (Lang *et al.,* 2018). Weight loss through diet and physical activity improves lung function, reduces symptoms, and decreases medication needs in obese asthmatics (Lang *et al.,* 2018). In addition, diets rich in antioxidants, omega-3 fatty acids, and vitamin D may reduce airway inflammation, although more research is needed to confirm their roles (Wood *et al.,* 2016).

Smoking Cessation and Air Quality

Smoking is a major exacerbating factor in asthma, leading to poor symptom control and reduced response to corticosteroids (Thomson, 2007). Smoking cessation significantly improves lung function and reduces exacerbations (Polosa *et al.,*). Additionally, improving indoor air quality by reducing exposure to volatile organic compounds (VOCs), nitrogen dioxide, and particulate matter can mitigate asthma symptoms, particularly in children (Mendell *et al.*, 2011).

2.8 USE OF OVALBUMIN (OVA) IN FEMALE SPRAGUE-DAWLEYS RATS

Animal models are essential tools in asthma research, allowing detailed study (González-González *et al.*, 2020). The ovalbumin (OVA)-induced asthma model is widely used to mimic human allergic asthma in female Sprague Dawley rats (Kim *et al.,* 2019). Ovalbumin, a glycoprotein found in egg whites, serves as a specific allergen to induce allergic airway inflammation and hyperresponsiveness (Chaudhary *et al.,* 2021). The experimental protocol involves sensitization of rats by intraperitoneal injection of OVA combined with an adjuvant, usually aluminum hydroxide (Zhao *et al*., 2018). After sensitization, rats are exposed to aerosolized OVA repeatedly, triggering airway inflammation and bronchial hyperresponsiveness (Ramos-Barbosa *et al.*, 2017). This method reliably induces eosinophilic infiltration, mucus hypersecretion, and airway obstruction (Yiamouyiannis *et al.*, 2018). These pathological features closely resemble those observed in human asthma (Kim *et al.,* 2019). The OVA model also exhibits a Th2-skewed immune response, characterized by increased levels of cytokines such as IL-4, IL-5, and IL-13 (Kim *et al.*, 2019). These cytokines mediate eosinophil recruitment and IgE production, central to allergic asthma pathogenesis (Kim *et al*., 2019).

CHAPTER THREE

RESEARCH DESIGN AND METHODOLOGY

3.1 EXPERIMENT ANIMALS

This study involved the use of 64 female Sprague-Dawley rats for a duration of seven (7) weeks. They all received proper animal care in line with international guidelines for experimental animal handling. Ethical approval obtained from the College of Medical Sciences ethics board. The Sprague-Dawley rats were housed in a clean, cool and sterile environment at 22 °C room temperature, they were kept in plastic cages, where they had access to food and water throughout the period of the experimental process.

3.2 MATERIALS

- Plastic cages
- Cutton wool
- Tissue paper
- Clean drinking water
- Feeding and drinking plates
- Dissection materials
- Feed
- Weighing balance
- Chloroform
- formaldehyde
- Nebulizer
- Gloves
- Plain bottles
- Saline solution
- Montelukast
- Salbutamol
- Prednisolone
- Ovalbumin
- Aluminium hydroxide
- Mentholated spirit
- Saw dust

3.3 STUDY DESIGN

Sprague-Dawley rats weighing 120-250 g were divided into two (2) main groups; the Control group and Test group. The control group was further divided into two (2) subgroups; the negative control and the positive control. All groups consists of eight (8) rats each. The negative control group only received normal rat chow and water throughout the experimental period, while the positive control group was exposed to concentrations of Ovalbumin (OVA, egg albumin grade II) to induce asthma, with no asthma treament. The test group was further divided into six (6) subgroups, also exposed to concentrations of Ovalbumin after which they were treated with salbutamol, prednisolone and montelukast.

3.4 EXPERIMENTAL PROTOCOL/DESIGN

This experiment was carried out in phases:

Phase 1

Rats were acclimatized into their new environment for two (2) weeks before which they were divided in to eight (8) groups.

GROUP 1: Negative control, not asthmatic and not treated

GROUP 2: Positive contol, asthmatic and not treated

GROUP 3: Asthmatic and treated with salbutamol

GROUP 4: Asthamatic and treated with montelukast

GROUP 5: Asthmatic and treated with prednisolone

GROUP 6: Asthmatic and treated with salbutamol and prednisolone

GROUP 7: Asthmatic and treated with montelukast and prednisolone

GROUP 8: Asthmatic and treated with salbutamol and montelukast

One control group and all test groups were induced with asthma following the modified guideline outlined by (Bai *et al*., 2019; Wu *et al.*, 2019) at the end of acclimatization, after which all groups were weighed. On the third week, all groups except the negative control group, were sensitized via intraperitoneal injection of 1mg ovalbumin (OVA), which was emulsified in 20mg of aluminium hydroxide [$Al(OH)_3$)] and dissolved in 0.9% of saline. They were sensitized with OVA on day one and seven of the third week.

From day 21, sensitized rats were challenged by exposure to aerosolized 1% OVA solution, in a plastic chamber measuring 70cm in diameter and 40cm in length

connected to a Medel family nebulizer (REF 90543 MEDEL FAMILY SILVER AEROSOL).

Asthma induction was verified first week after challenge with evidence of neutrophilia and eosinophilia in all test groups compared to control group (Bai *et al*., 2019; Wu *et al*., 2019).

Phase 2

Treatment began with 1mg/ml salbutamol, 10mg/ml montelukast, 3mg/ml prednisolone. Treatment lasted the period of challenge (28 days/ 4 weeks).

Phase 3

At the end of treatment period, all animals were weighed and thereafter anesthetized by exposure to chloroform. Blood and tissue samples were collected for biomarker analysis and histological examination.

3.5 HISTOLOGICAL ANALYSIS

Brain, heart, aorta, kidney, and lung tissues were fixed in 10% (v/v) formaldehyde solution, and subsequently embedded in paraffin. The specimens were sectioned and stained with haematoxylin and eosin (H&E) dye. Images of selected sections were captured at 10X magnification using a zoom digital camera (Bancroft *et al.,* 2020; Suvarna *et al.*, 2018).

3.6 BLOOD SAMPLING AND SERUM ISOLATION

Blood was collected from the retro-orbital plexus of rats under light diethyl ether anaesthesia, using non-heparinized tubes. The samples were kept at room temperature for about 30 minutes to allow clotting, then centrifuged at 5000 rpm for 15 minutes. The serum obtained was carefully stored and frozen for later quantitative analysis of selected biomarkers (Giknis *et al.,* 2008).

3.7 STATISTICAL ANALYSIS

All the results are shown as the mean ± standard error of the mean (SEM). Data were analyzed using a one-way analysis of variance (ANOVA) to check for differences between the groups, and then used Tukey’s post hoc test for pairwise comparisons.

The analysis was done with GraphPad Prism version 10.0.3 (GraphPad Software, San Diego, CA), and values of $p < 0.05$ were taken to show statistical significance.

CHAPTER 4

RESULTS

4.1: Results Of Statistical Analysis

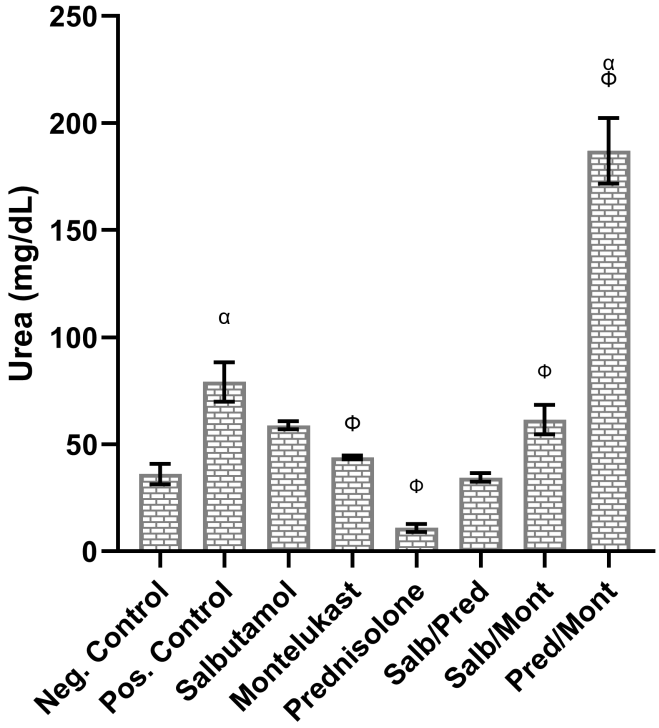

Figure 4: Effect of salbutamol, montelukast, prednisolone, and their combinations on serum urea concentration

Results show a statistically significant increase in serum urea concentration in the prednisolone/montelukast-treated group compared with the negative controls. ($p<0.05$), but no statistically significant difference among the positive control, salbutamol, montelukast, prednisolone, salbutamol/prednisolone, and salbutamol/montelukast-treated groups compared with the negative control ($p>0.05$). Also, there was a statistically significant decrease in the montelukast, prednisolone, salbutamol/montelukast, and prednisolone/montelukast-treated groups compared to the positive control ($p<0.05$). n=4 ± SEM. $^{\alpha}p<0.05$ compared to negative control; $^{\Phi}p<0.05$ compared to positive control.

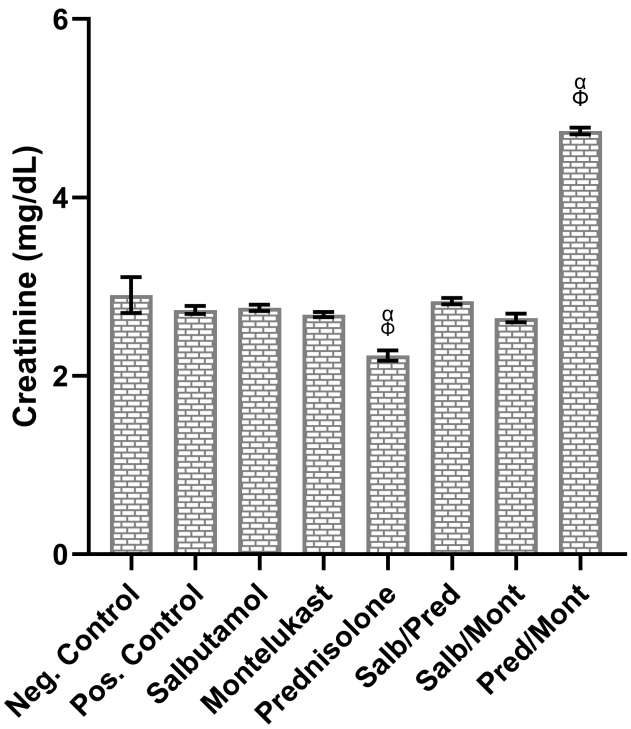

Figure 5: Effect of salbutamol, montelukast, prednisolone, and their combinations on serum creatinine concentration

Results show a statistically significant increase in serum creatinine concentration in the prednisolone/montelukast-treated group, and a decrease in the prednisolone-treated group compared with the negative and positive controls. ($p<0.05$), but no statistically significant difference among the positive control, salbutamol, montelukast, salbutamol/prednisolone, and salbutamol/montelukast-treated groups compared with the negative control ($p>0.05$). n=4 ± SEM. $^{\alpha}p<0.05$ compared to negative control; $^{\Phi}p<0.05$ compared to positive control.

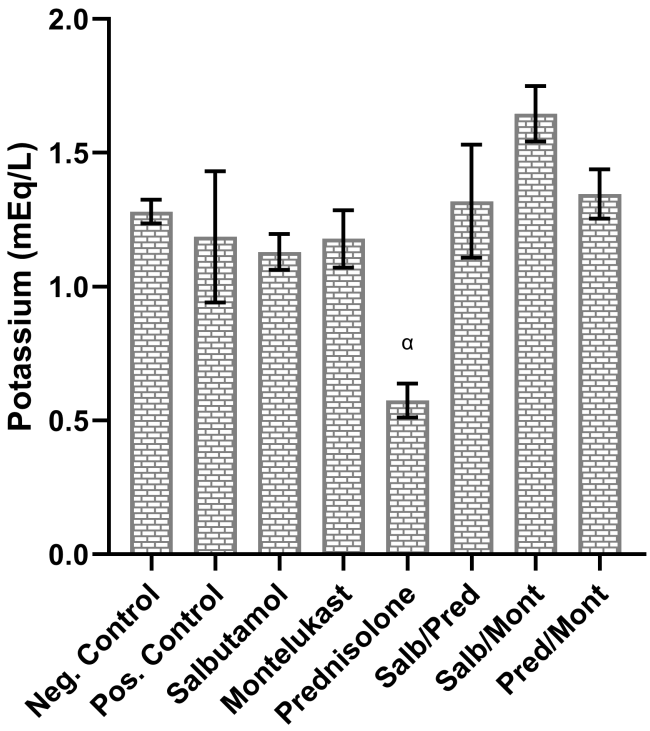

Figure 6: Effect of salbutamol, montelukast, prednisolone, and their combinations on serum potassium ion concentration

Results show a statistically significant decrease in serum potassium ion concentration in the prednisolone-treated group compared with the negative controls. ($p<0.05$), but no statistically significant difference among the positive control, salbutamol, montelukast, salbutamol/prednisolone, salbutamol/montelukast, and prednisolone/montelukast-treated groups compared with the negative control ($p>0.05$). n=4 ± SEM. $^{\alpha}p<0.05$ compared to negative control; $^{\Phi}p<0.05$ compared to positive control.

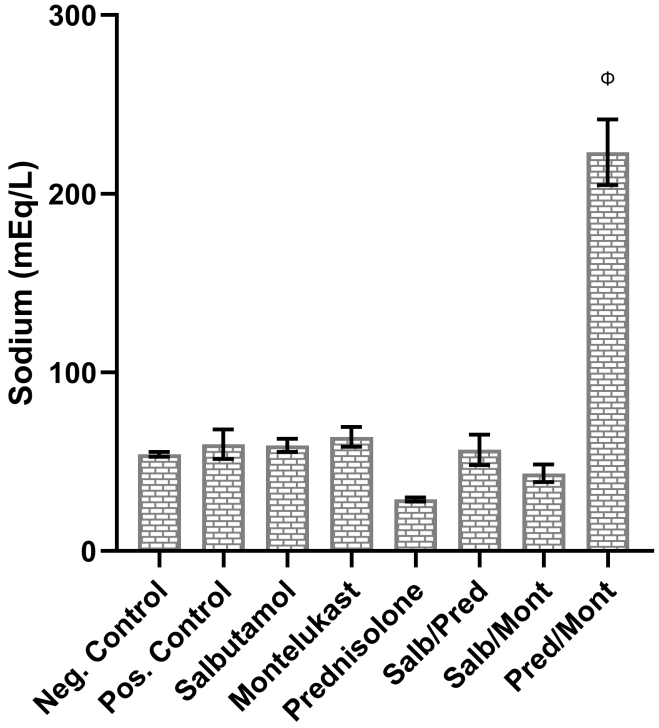

Figure 7: Effect of salbutamol, montelukast, prednisolone, and their combinations on serum sodium ion concentration

Results show no statistically significant decrease in serum sodium ion concentration in all groups compared with the negative controls ($p>0.05$). Also, there was a statistically significant increase in the prednisolone/montelukast-treated group compared to the positive control ($p<0.05$). in the n=4 ± SEM. $^{\alpha}p<0.05$ compared to negative control; $^{\Phi}p<0.05$ compared to positive control.

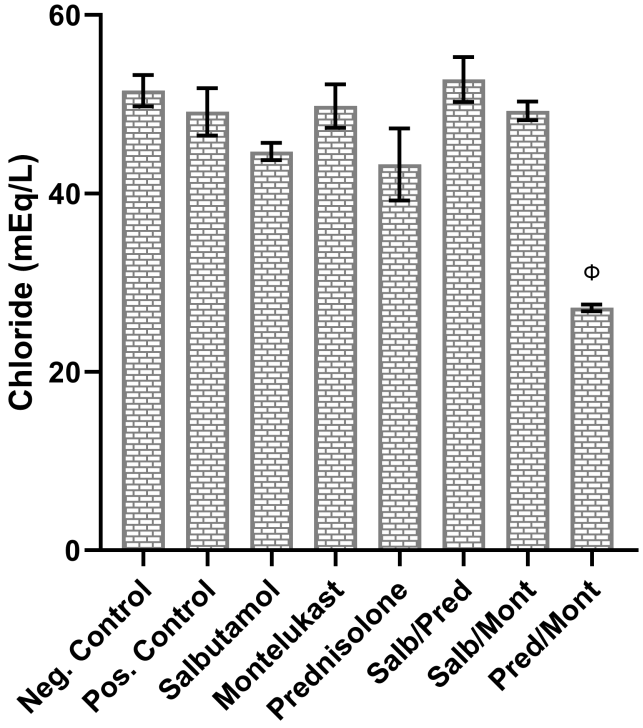

Figure 8: Effect of salbutamol, montelukast, prednisolone, and their combinations on serum chloride ion concentration

Results show no statistically significant decrease in serum chloride concentration in all groups compared with the negative controls ($p>0.05$). Also, there was a statistically significant decrease in the prednisolone/montelukast-treated group compared to the positive control ($p<0.05$). in the n=4 ± SEM. $^{\alpha}p<0.05$ compared to negative control; $^{\Phi}p<0.05$ compared to positive control.

CHAPTER 5
DISCUSSION AND CONCLUSION

5.1 DISCUSSION

This study examined the effects of salbutamol, montelukast, prednisolone, and their combinations on kidney function by measuring serum urea, creatinine, and electrolytes. The results show that although these drugs are mainly used for the treatment of asthma, they can also influence kidney function and the balance of electrolytes in the body. This suggests that asthma medications may have effects that go beyond the respiratory system.

One important finding in this study was the significant increase in serum urea and creatinine levels in the group treated with the combination of prednisolone and montelukast when compared to both the negative and positive control groups. This increase may indicate that the combination of these two drugs could cause some stress on the kidneys or slightly reduce their ability to remove waste products efficiently. The observation suggests that using corticosteroids like prednisolone together with leukotriene antagonists such as montelukast may produce a stronger effect on kidney function than when each drug is used alone. This may be due to how both drugs affect kidney blood flow and the way the kidney filters or reabsorbs substances.

On the other hand, treatment with prednisolone alone caused a decrease in serum creatinine and potassium levels compared with the control groups. This is consistent with the known effect of corticosteroids on kidney function, as they tend to increase the loss of potassium in urine and alter electrolyte regulation. The reduction in creatinine level could mean that prednisolone improves the rate at which the kidneys filter blood, which is similar to the effect seen with mild diuretic drugs that promote fluid excretion.

The groups treated with salbutamol and montelukast alone did not show any major changes in serum urea, creatinine, or electrolytes compared with the control groups. This indicates that both drugs are relatively safe for kidney function when used separately. The small decrease in urea and creatinine levels observed in the montelukast group, compared to the positive control, might suggest that montelukast has a mild protective or balancing effect on the kidneys, but this would need further studies to confirm.

The combination treatments produced different outcomes. The groups treated with salbutamol/prednisolone and salbutamol/montelukast did not show major differences

in kidney markers or electrolyte levels compared with the control groups. However, the prednisolone/montelukast combination caused clear increases in urea and creatinine levels, as well as some changes in sodium and chloride levels. These findings suggest that while most combinations are not harmful, using prednisolone and montelukast together may lead to slight imbalances in kidney function and electrolyte levels.

Overall, these results suggest that while the individual drugs salbutamol, montelukast, and prednisolone, are generally safe for kidney function, combining prednisolone and montelukast could have a greater impact on the kidneys. It is therefore important to monitor kidney health when patients are placed on such combined therapies. Future research involving kidney tissue examination and oxidative stress markers would help to better understand how these drugs cause these changes in kidney function.

5.2 Conclusion

This study shows that salbutamol, montelukast, and prednisolone affect kidney function and electrolyte balance in different ways. When used alone, each drug caused little or no significant change in serum urea, creatinine, or electrolytes. However, the combination of prednisolone and montelukast led to increased levels of urea and creatinine, suggesting some level of kidney stress or reduced kidney efficiency. These results highlight the need for careful use of these drugs in combination and the importance of monitoring kidney function during treatment, especially for patients on long-term therapy.

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