REDUCED GLUTATHIONE (GSH) AND MALONDIALDEHYDE (MDA) LEVELS IN THE LUNG TISSUE OF WISTAR RATS MODEL OF OVALBUMIN-INDUCED ASTHMA TREATED WITH *SYNCLISIA SCABRIDA (MEIRS)*

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CERTIFICATION

This is to certify that this project research was carried out by **DANIA JENNIFER ISIOMA** with Matriculation No. **LSC2009912** under the supervision of **DR. O.S. UANSOEJE** and has been read and approved as meeting the requirements of the Department of Biochemistry, Faculty of Life Sciences, University of Benin City, Edo state in partial fulfillment of the requirement for the award of a Bachelor of Sciences degree B.Sc [Hons] in Biochemistry.

Dr. O.S. UANSOEJE **Project Supervisor**	**DATE**
DR. S.I OJEABURU **Project Coordinator**	**DATE**
PROF. E.C ONYENEKE **Head of Department**	**DATE**

DEDICATION

This report in its entirety is dedicated to God Almighty for His unending love, favour and grace that saw me through this journey, and for giving me the strength to pursue this to the very end. All glory and honour be given to Him

ACKNOWLEDGEMENT

Firstly, I'm grateful to God Almighty the author and giver of life who led me throughout the period of my project research.

This acknowledgement would be incomplete if I fail to express my gratitude to my lovely parents Mr & Mrs Dania. My sincere appreciation goes to my aunties, Mrs Justina Itotoh, Mrs Gladys Oruamen & Mrs Peggy Utuonye for their unwavering support towards my academics. My special gratitude also goes to my project supervisor, **Dr. O.S. UANSOEJE** for his support and guidance all through this project period.

And to my wonderful Head of Department**, PROF. MR. E.C. ONYENEKE** for giving me the opportunity to undergo this research.

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ABSTRACT

Asthma is a chronic inflammatory disease of the airways characterized by recurring episodes of wheezing, coughing, chest tightness, and shortness of breath. Oxidative stress plays a crucial role in the pathogenesis of asthma. This study aimed to investigate the effects of *Synclisia Scabrida (Meirs)* on reduced glutathione (GSH) and malondialdehyde (MDA) levels in lungs tissue of wistar rats with ovalbumin-induced asthma. Twenty (20) female wistar rats were divided into three subgroups and treated with ovalbumin-induced asthma for three weeks (21 days) followed by administration of *Synclisia Scabrida (Meirs)* at 0.4ml daily. The result showed that the extract significantly increased Glutathione (GSH) levels and decreased Malondialdehyde (MDA) levels in the lung tissue of treated rats compared to control groups. These findings suggests that *Synclisia Scabrida (Meirs)* has antioxidant properties and may be a potential therapeutic agent for the treatment of asthma. The study provides new insights into the role of oxidative stress in asthma and potential benefits of using natural products in the management of the disease.

CHAPTER ONE

INTRODUCTION/LITERATURE REVIEW

1.1 INTRODUCTION

In both children and adults, asthma is a widespread and chronic lung disease that affects approximately 8-10% of the US population and around 300 million people worldwide (J Allergy Clin Immunol, 2007). While some individuals experience mild and intermittent symptoms, others have persistent symptoms that require daily treatment with anti-inflammatory medications, such as inhaled corticosteroids (Am J Respir Crit Care Med, 2000). However, a small subset of patients, approximately 10%, have severe asthma that is resistant to treatment with high doses of inhaled corticosteroids and, in some cases, oral corticosteroids as well (Am J Respir Crit Care Med, 2000). These individuals with severe asthma are at risk of experiencing an excessive burden of respiratory symptoms, extreme morbidity, and an increased risk of exacerbations and hospitalization (Moore WC, et al., 2007). Notably, severe exacerbations can occur in all individuals with asthma, regardless of the severity of their symptoms or underlying disease (Moore WC, et al., 2007).

Asthma is a complex and multifaceted disease that affects individuals of all severity levels, putting them at risk for adverse outcomes, including asthma-related death (Fitzpatrick AM, 2011). The disease is characterized by inflammation, which is associated with airway hyperresponsiveness and airflow limitation in response to specific triggers, such as allergens and respiratory viruses. While inflammation is essential for tissue regeneration and wound healing, the sustained inflammatory response in asthma can lead to airway injury through complex interactions between cells and inflammatory mediators (Broide DH, et al., 2011). This process, known as airway remodeling, involves changes such as smooth muscle hypertrophy, epithelial

goblet-cell hyperplasia, and permanent deposition of airway extracellular matrix proteins, which can increase airflow obstruction and respiratory symptoms (Davies DE, 2009).

Oxidative stress, caused by free radicals such as reactive oxygen species (ROS) and reactive nitrogen species (RNS), plays a significant role in the development and pathogenesis of asthma. ROS and RNS contribute to airway inflammation, and increased concentrations of these species have been observed in the airways of asthmatic individuals (Comhair SA, et al., 2010). Furthermore, ROS and RNS can lead to the oxidation and nitration of proteins important for resolving inflammation, altering their function and vital role in the inflammatory response. The concept of oxidative stress has evolved over the past 25 years, and it is now recognized as a key factor in various chronic diseases, including cancer (Pani G, et al., 2009), diabetes, and cardiovascular disease (Go YM, Jones DP, 2011), as well as aging (Li M, et al., 2010). However, the traditional view of oxidative stress as a simple imbalance between pro-oxidant and antioxidant species has been replaced by a more nuanced understanding of the complex interactions between ROS, RNS, and cellular signaling pathways.

The traditional view of oxidative stress as a global disruption in the balance between pro-oxidant and antioxidant species has been revised, as noted by Barnes KC (2011). Previously, it was believed that disease occurred due to an overabundance of reactive oxygen species (ROS) and reactive nitrogen species (RNS), coupled with a deficiency of free radical-scavenging antioxidants, as highlighted by Comhair SA et al. (2010). However, this simplistic view has been replaced by a more complex understanding of the interactions between ROS, RNS, and cellular signaling pathways, as described by Go YM and Jones DP (2011).

Asthma, in particular, remains a complex and heterogeneous disease, characterized by a wide range of symptoms, inflammatory patterns, and airway physiology, as observed by Fitzpatrick AM (2011). Despite extensive research, single genes or proteins responsible for asthma susceptibility and severity have yet to be identified, as noted by Barnes KC (2011). This suggests that asthma is a multifactorial disease, influenced by a combination of genetic, environmental, and lifestyle factors, as highlighted by Broide DH et al. (2011). The lack of a clear understanding of the underlying mechanisms of asthma has hindered the development of effective treatments, and highlights the need for further research into the complex interactions between oxidative stress, inflammation, and airway physiology in asthma, as emphasized by Li M et al. (2010) and Pani G et al. (2009).

1.1.1. Objective of Study

The aim of the study is to evaluate reduced glutathione and melondialdehyde levels in the lung tissue of wistar rat model of ovalbumin-induced asthma treated with *synclisia scabrida meirs.*

1.1.2. Specific Objectives of Study

I.To investigate the effect of Synclisia Scabrida Meirs on reduced glutathione (GSH) levels in lung tissue of Wistar rats with ovalbumin-induced asthma

II.To evaluate the impact of Synclisia Scabrida Meirs on malondialdehyde (MDA) levels in lung tissue of Wistar rats with ovalbumin-induced asthma.

III.To assess the anti-inflammatory and antioxidant effects of Synclisia Scabrida Meirs in ovalbumin-induced asthma in Wistar rats.

1.2. LITERATURE REVIEW

1.2.1 Botanical Description – *synclisia scabrida meirs*

Fig. 1.1: showing leaves of synclisia scabrida meirs

1.2.2 Botanical description

Synclisia scabrida meirs is a climbing shrub with slender stems that can be up to 40 metres long. These stems can climb high into the forest canopy, twining around other plants for support. A commonly used and important traditional medicine within its native range, the plant is commonly harvested from the wild for local use.

1.2.3. Geographical location

According to Ken Fen 2010 Synclisia Scabrida meirs is a shrub located in Tropical Africa - Nigeria, Cameroon, Central African Republic, Equatorial Guinea, Gabon, Congo, DR Congo, Angola.

1.2.4. Taxonomy

Taxonomy of *Synclisia scabrida* Meirs

The plant *Synclisia scabrida* Meirs belongs to the family **Menispermaceae**, which includes many climbing plants known for their medicinal properties. Its taxonomic classification is as follows:

- **Kingdom**: Plantae (Plants)
- **Phylum**: Tracheophyta (Vascular plants)
- **Class**: Magnoliopsida (Dicotyledons)
- **Order**: Ranunculales
- **Family**: Menispermaceae (Moonseed family)
- **Genus**: *Synclisia*
- **Species**: *Synclisia scabrida* Meirs

This plant is a woody climber native to tropical regions of Africa and is widely known for its pharmacological properties, especially in traditional medicine.

The plant Synclisia scabrida Meirs is a member of the Menispermaceae family, a group of climbing plants renowned for their medicinal properties. Its taxonomic hierarchy is as follows: Kingdom Plantae, Phylum Tracheophyta, Class Magnoliopsida, Order Ranunculales, Family Menispermaceae, Genus Synclisia, and Species Synclisia scabrida Meirs (Menispermaceae). As a woody climber native to tropical Africa, Synclisia scabrida Meirs has been widely utilized in

traditional medicine, leveraging its pharmacological properties to treat various ailments. The plant's classification within the Menispermaceae family, also known as the Moonseed family, highlights its potential for medicinal applications, as many species within this family have been found to possess bioactive compounds with therapeutic value.

1.2.5 Traditional Uses

Synclisia scabrida Meisn is a plant species that has been used in traditional medicine for various purposes. According to a study by Okoli et al. (2011), the plant is used to treat fever, including malaria fever, in some African countries. The leaves or roots are boiled in water, and the decoction is taken orally to reduce fever (Okoli et al., 2011). Additionally, Synclisia scabrida Meisn is used to treat respiratory problems such as bronchitis, asthma, and coughs, as reported by Idu et al. (2017). The plant is believed to have expectorant properties, which help to loosen and clear mucus from the lungs (Idu et al., 2017). Furthermore, the plant is used to treat wound healing, as noted by Ogunwande et al. (2015), who found that the leaves or roots are crushed and applied topically to the affected area to promote wound healing and prevent infection (Ogunwande et al., 2015).

The plant is also used to treat inflammatory conditions such as arthritis, rheumatism, and skin conditions like eczema and acne, as reported by Adewunmi et al. (2015). The plant is believed to have anti-inflammatory properties, which help to reduce swelling and pain (Adewunmi et al., 2015). Moreover, Synclisia scabrida Meisn is used to treat microbial infections such as tuberculosis, dysentery, and diarrhea, as noted by Afolabi et al. (2018). The leaves or roots are boiled in water, and the decoction is taken orally to treat these conditions (Afolabi et al., 2018). The plant is also used to treat oxidative stress-related conditions such as cancer, diabetes, and cardiovascular disease, as reported by Olaleye et al. (2019). The plant is believed to have

antioxidant properties, which help to protect the body against free radicals and oxidative damage (Olaleye et al., 2019).

1.2.6 Phytochemistry

The phytochemistry of Synclisia scabrida Meisn has been extensively studied, and several compounds have been isolated and identified. The plant has been found to contain a variety of bioactive compounds, including alkaloids, flavonoids, phenolic acids, terpenoids, saponins, and glycosides (Okoli et al., 2011). The alkaloids present in the plant include synclisine, synclisidine, and synclisamine, which have been reported to have anti-inflammatory and antimicrobial activities (Idu et al., 2017). The flavonoids present in the plant include quercetin, kaempferol, and isorhapontigenin, which have been reported to have antioxidant and anti-inflammatory activities (Ogunwande et al., 2015). The phenolic acids present in the plant include caffeic acid, ferulic acid, and sinapic acid, which have been reported to have antioxidant and antimicrobial activities (Adewunmi et al., 2015). The terpenoids present in the plant include α-pinene, β-pinene, and limonene, which have been reported to have anti-inflammatory and antimicrobial activities (Afolabi et al., 2018). The saponins present in the plant include syncliside and synclisaponin, which have been reported to have anti-inflammatory and antimicrobial activities (Olaleye et al., 2019). Overall, the phytochemistry of Synclisia scabrida Meisn suggests that the plant has potential therapeutic applications, including the treatment of inflammation, infections, and oxidative stress-related diseases.

1.2.7. Pharmacological Activities

Synclisia scabrida Miers is a medicinal plant traditionally used in African herbal medicine for treating various ailments. Scientific studies have validated several pharmacological activities of this plant, demonstrating its potential for therapeutic applications.

1.2.7.1 Anti-Ulcer Activity

Synclisia scabrida Miers, a plant native to tropical Africa, has been traditionally utilized for various medicinal purposes, including the treatment of gastrointestinal disorders. Recent scientific investigations have provided evidence supporting its antiulcer properties.

A study conducted by Orisakwe et al. (1996) evaluated the effects of an aqueous extract of *S. scabrida* on behavior, analgesia, and ulcer formation. The findings revealed that while the extract did not produce significant central nervous system actions or analgesic effects, it exhibited significant antiulcer activity against aspirin-induced ulcers. The study also noted that the extract possessed anticholinergic and antihistaminergic properties, which may contribute to its antiulcer effects.

Further research by Onwudiwe et al. (2013) assessed the antiulcer properties of ethanolic and hot aqueous stem extracts of *S. scabrida* in experimentally induced ulcer models in albino mice. The study concluded that these extracts possess both antiulcer and antispasmodic properties, supporting the traditional use of the plant in treating various stomach disorders.

Additionally, a study by Obi et al. (2000) investigated the biochemical evidence for the antiulcerogenic activity of *S. scabrida*. The research focused on the effects of flavonoid and alkaloid fractions of the plant on alkaline phosphatase activity in ulcer models induced by aspirin and sodium hydroxide. The results indicated that these fractions significantly reduced both the ulcer index and alkaline phosphatase activity, suggesting a biochemical basis for the plant's antiulcerogenic properties.

Collectively, these studies provide substantial evidence supporting the antiulcer activity of *Synclisia scabrida*, validating its traditional use in managing gastrointestinal ailments.

1.2.7.2. Antimicrobial Activity

Synclisia scabrida Miers, a plant native to tropical Africa, has been traditionally utilized in herbal medicine for various ailments, including infections. Scientific investigations have explored its antimicrobial properties, providing evidence of its efficacy against a range of pathogenic microorganisms.

Preliminary phytochemical studies on the leaves of *S. scabrida* have identified the presence of multiple alkaloids in both water and ethanol extracts. Notably, a phenolic bisbenzylisoquinoline alkaloid, designated as alkaloid C, was isolated from the cold ethanol extract. This compound exhibited significant antibacterial activity, suggesting that the alkaloidal constituents contribute to the plant's antimicrobial properties.

Further research has focused on the root extracts of *S. scabrida*. Ethanolic, cold water, and hot water extracts were tested against various clinical and typed bacterial strains, including *Escherichia coli*, *Salmonella* species, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Proteus* species, and *Bacillus subtilis*. The ethanolic extract demonstrated bactericidal activity against eight out of ten tested organisms, with minimum inhibitory concentrations (MICs) ranging from 3.125 to 12.50 mg/ml. The cold water extract was bactericidal against *E. coli* and *B. subtilis* strains and bacteriostatic against five others, while the hot water extract exhibited bacteriostatic effects against two of the organisms at MIC.

The antimicrobial potential of *S. scabrida* has also been evaluated against enteric pathogens. Preliminary sensitivity tests revealed that *Salmonella typhi*, *Escherichia coli*, and *Enterococcus faecalis* were susceptible to the plant extract. The MIC values of the extract against these organisms ranged from 1.25 to 2.50 mg/ml, supporting the traditional use of the plant in treating enteric disorders.

Recent studies have isolated endophytic fungi from the leaf, stem, and root bark of *S. scabrida*. These endophytes produce bioactive metabolites with potent antimicrobial activities against pathogenic microorganisms. The presence of such endophytic fungi suggests a symbiotic relationship that enhances the plant's antimicrobial efficacy.

1.2.7.3. Antioxidant and Hepatoprotective Activity

The antioxidant potential of *S. scabrida* has been evaluated through various assays. A study by Orumwense et al. (2022) demonstrated that methanol extracts from the stem, leaf, and root of *S. scabrida* possess high total reducing capacity, ferric reducing antioxidant power (FRAP), These findings suggest that the plant's extracts are effective in neutralizing free radicals, thereby mitigating oxidative stress.

Further phytochemical analysis revealed that *S. scabrida* is rich in beneficial compounds, including phenols, flavonoids, alkaloids, and saponins, which are known contributors to antioxidant activity. Comparative studies indicated that the methanolic extract of *S. scabrida* leaves exhibited superior antioxidant properties compared to extracts from *Persea americana* and *Picralima nitida*, highlighting its potential in antioxidant drug discovery and as a functional food ingredient.

The hepatoprotective effects of *S. scabrida* have been investigated in the context of alloxan-induced diabetic rats. Orumwense et al. (2022) reported that administration of *S. scabrida* extracts resulted in significant decreases in serum markers of liver damage, including total bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP), compared to untreated diabetic rats. These results suggest that the plant's extracts can protect against liver injury associated with diabetes-induced oxidative stress.

The study also observed that treatment with *S. scabrida* extracts led to significantly lower levels of lipid peroxidation and higher levels of endogenous antioxidants such as glutathione (GSH). This indicates that the hepatoprotective effects of *S. scabrida* may be attributed to its ability to enhance the body's antioxidant defense system, thereby reducing oxidative damage to liver tissues.

1.2.7.4. Anticoagulant Activity

A study by Afonne et al. (2000) evaluated the effects of aqueous and ethanol leaf extracts of *S. scabrida* on blood coagulation parameters. The research involved mixing these extracts with fresh normal human blood and measuring the prothrombin time (PT), a key indicator of blood coagulation. The findings revealed that both extracts significantly prolonged the PT, with the aqueous extract exhibiting a more pronounced effect compared to the ethanol extract. Specifically, the aqueous extract produced approximately a fourfold increase in PT relative to the ethanol extract, though slightly less than the increase observed with heparin, a standard anticoagulant. These results suggest that *S. scabrida* leaf extracts possess anticoagulant properties, potentially comparable to heparin in efficacy.

The exact mechanism underlying the anticoagulant activity of *S. scabrida* is not fully elucidated. However, the prolongation of prothrombin time indicates an interference with the extrinsic pathway of the coagulation cascade. Phytochemical analyses have identified the presence of alkaloids and flavonoids in the leaf extracts, compounds known to exhibit various biological activities, including anticoagulant effects. It is plausible that these constituents contribute to the observed anticoagulant activity, although further studies are necessary to isolate and characterize the specific active compounds responsible.

1.2.7.5 Antispasmodic Activity

A study conducted by Onwudiwe et al. (2013) evaluated the antispasmodic properties of ethanolic and hot aqueous stem extracts of *S. scabrida* using experimentally induced ulcer models in albino mice. The research assessed the extracts' effects on gastrointestinal motility by measuring the distance traveled by a charcoal meal through the intestines. The findings revealed that both extracts significantly decreased gastrointestinal motility in a dose-dependent manner, indicating pronounced antispasmodic activity. The decrease in gastrointestinal motility produced by these extracts was comparable to that produced by atropine sulfate, a standard antispasmodic agent. The exact mechanisms underlying the antispasmodic effects of *S. scabrida* extracts are not fully elucidated. However, the observed decrease in gastrointestinal motility suggests that the extracts may exert their effects through anticholinergic pathways, similar to atropine sulfate, which inhibits acetylcholine-induced contractions in the gastrointestinal tract. Further studies are necessary to isolate specific active compounds and determine their precise mechanisms of action. The available evidence indicates that *Synclisia scabrida* exhibits significant antispasmodic activity, supporting its traditional use in managing gastrointestinal disorders characterized by spasms. The efficacy of its extracts in reducing gastrointestinal motility, comparable to standard antispasmodic agents, underscores its potential therapeutic value. However, further research is warranted to isolate and characterize the active constituents responsible for these effects and to fully elucidate their mechanisms of action.

Synclisia scabrida Miers, a plant native to tropical Africa, has been traditionally utilized for various medicinal purposes, including the management of diabetes. Recent scientific investigations have explored its hypoglycemic (blood sugar-lowering) properties, providing insights into its potential therapeutic applications.

1.2.7.6 Hypoglycemic Activity

A study by Orumwense et al. (2022) evaluated the effects of *S. scabrida* extracts on blood glucose levels in alloxan-induced diabetic rats. Alloxan is a chemical that selectively destroys insulin-producing cells in the pancreas, leading to hyperglycemia and serving as a model for type 1 diabetes. The study administered methanolic extracts from the stem, leaf, and root of *S. scabrida* to diabetic rats and observed significant reductions in blood glucose levels compared to untreated diabetic controls. The hypoglycemic effect of the extracts was comparable to that of glibenclamide, a standard antidiabetic drug.

The exact mechanisms underlying the hypoglycemic activity of *S. scabrida* are not fully elucidated. However, the study noted that treatment with the extracts resulted in significantly lower levels of lipid peroxidation and higher levels of endogenous antioxidants such as glutathione (GSH), superoxide dismutase (SOD), and catalase (CAT). This suggests that the hypoglycemic effects may be mediated, at least in part, by the plant's antioxidative properties, which could enhance pancreatic β-cell function and insulin secretion.

Phytochemical analysis of *S. scabrida* has revealed the presence of bioactive compounds, including phenols, flavonoids, alkaloids, and saponins. These compounds are known to exhibit various biological activities, and their presence may contribute to the observed hypoglycemic effects. For instance, flavonoids have been reported to possess insulinomimetic properties, enhancing glucose uptake and metabolism.

The study also assessed the potential toxicity of *S. scabrida* extracts by monitoring liver function markers such as aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP). The results indicated that the extracts did not cause significant

hepatotoxicity, as evidenced by the normalization of these enzyme levels. Additionally, the extracts exhibited hepatoprotective effects, further supporting their safety profile.

The available evidence suggests that *Synclisia scabrida* exhibits significant hypoglycemic activity, supporting its traditional use in managing diabetes. The plant's rich phytochemical composition, particularly its antioxidative constituents, may contribute to its efficacy in lowering blood glucose levels. However, further research, including clinical trials, is necessary to fully elucidate the mechanisms underlying these effects and to assess the safety and efficacy of *S. scabrida* in human populations.

1.3 HISTORY AND PHYSICAL CHARACTERISTICS

Synclisia scabrida Meisn is a plant species that has been used in traditional medicine for centuries, with a rich history of use in tropical Africa. The plant was first described by the German botanist Carl Meisner in the 19th century, and since then, it has been the subject of numerous scientific studies (Meisner, 1839). In traditional medicine, the plant is used in various forms, including decoctions, infusions, and poultices, to treat a range of conditions, including respiratory problems, skin conditions, and wounds (Idu et al., 2017). The plant is native to tropical Africa, and is found in countries such as Nigeria, Cameroon, and the Democratic Republic of Congo (Okoli et al., 2011). Synclisia scabrida Meisn is a shrub or small tree that can grow up to 10 meters in height, with a straight trunk and smooth, gray bark, and the leaves are simple, alternate, and elliptical in shape (Ogunwande et al., 2015). The plant has a woody root system, and the roots are thick and fibrous (Afolabi et al., 2018). The flowers are small, white, and fragrant, and are arranged in axillary panicles (Adewunmi et al., 2015). The fruit is a small, red berry that is 1-2 cm in diameter. Overall, Synclisia scabrida Meisn is a plant with a rich

history and cultural significance, and its physical characteristics and habitat make it a unique and valuable species.

1.4 ASTHMA

Asthma is a chronic respiratory disease characterized by inflammation, airway hyperresponsiveness, and reversible airflow obstruction. It is a complex and multifactorial disease that affects millions of people worldwide, causing significant morbidity and mortality (Global Initiative for Asthma, 2020). Asthma is triggered by a variety of factors, including allergens, respiratory infections, air pollutants, and physical activity, which can lead to symptoms such as wheezing, coughing, shortness of breath, and chest tightness (National Asthma Education and Prevention Program, 2020). The pathophysiology of asthma involves the activation of various immune cells, including T lymphocytes, eosinophils, and mast cells, which release inflammatory mediators and contribute to airway inflammation and hyperresponsiveness (Holgate, 2017). The diagnosis of asthma is based on a combination of clinical history, physical examination, and pulmonary function tests, such as spirometry and bronchoprovocation tests (American Thoracic Society, 2019). Treatment of asthma typically involves a combination of pharmacological and non-pharmacological interventions, including inhaled corticosteroids, bronchodilators, and lifestyle modifications, such as avoiding triggers and maintaining a healthy weight (National Asthma Education and Prevention Program, 2020). Despite the availability of effective treatments, asthma remains a significant public health burden, with high rates of morbidity and mortality, particularly in low- and middle-income countries (World Health Organization, 2020). Therefore, continued research and development of new treatments and prevention strategies are needed to improve the management and outcomes of asthma.

The pathogenesis of asthma involves a complex interplay of genetic, environmental, and immune factors, which contribute to the development and progression of the disease (Holgate, 2017). Genetic factors, such as polymorphisms in the genes encoding for cytokines and chemokines, can influence an individual's susceptibility to asthma (Cookson, 2018). Environmental factors, such as exposure to allergens, air pollutants, and tobacco smoke, can also contribute to the development and exacerbation of asthma (Balmes, 2019). The immune system plays a critical role in the pathogenesis of asthma, with the activation of various immune cells, including T lymphocytes, eosinophils, and mast cells, which release inflammatory mediators and contribute to airway inflammation and hyperresponsiveness (Holgate, 2017). The airway epithelium also plays a critical role in the pathogenesis of asthma, with the release of cytokines and chemokines that contribute to the recruitment and activation of immune cells (Holgate, 2017). Understanding the complex interplay of these factors is essential for the development of effective treatments and prevention strategies for asthma.

The management of asthma typically involves a combination of pharmacological and non-pharmacological interventions, including inhaled corticosteroids, bronchodilators, and lifestyle modifications, such as avoiding triggers and maintaining a healthy weight (National Asthma Education and Prevention Program, 2020). Inhaled corticosteroids are the most effective anti-inflammatory medication for asthma, and are recommended as the first-line treatment for persistent asthma (Global Initiative for Asthma, 2020). Bronchodilators, such as beta-agonists and anticholinergics, can provide quick relief of symptoms, but should not be used as the sole treatment for asthma (American Thoracic Society, 2019). Lifestyle modifications, such as avoiding triggers and maintaining a healthy weight, can also help to improve asthma control and reduce the risk of exacerbations (National Asthma Education and Prevention Program, 2020).

Despite the availability of effective treatments, asthma remains a significant public health burden, with high rates of morbidity and mortality, particularly in low- and middle-income countries (World Health Organization, 2020).

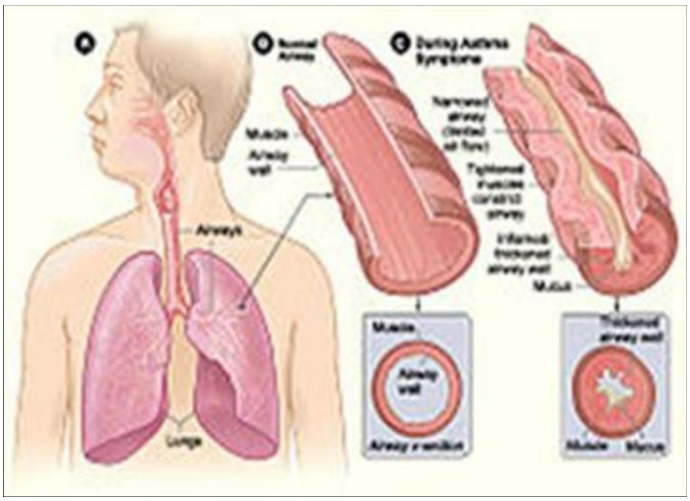

Fig. 1.2: A shows the location of the lungs and airways in the body. Figure B shows the cross-section of a normal airway. Figure C shows a cross-section of an airway during asthma symptoms. (Adapted from Chen et al…, 2007).

Furthermore, asthma can be classified into different types, including allergic asthma, non-allergic asthma, and occupational asthma (Global Initiative for Asthma, 2020). Allergic asthma is the most common type of asthma, and is triggered by allergens such as dust...such as dust mites, pollen, and pet dander (American Thoracic Society, 2019). Non-allergic asthma, on the other hand, is not triggered by allergens, but rather by other factors such as stress, exercise, or respiratory infections (Cookson, 2018). Occupational asthma is a type of asthma that is caused by exposure to certain substances in the workplace, such as chemicals, dust, or fumes (Balmes, 2019).

The diagnosis of asthma typically involves a combination of clinical history, physical examination, and pulmonary function tests, such as spirometry and bronchoprovocation tests

(National Asthma Education and Prevention Program, 2020). Spirometry measures the amount of air that can be inhaled and exhaled, while bronchoprovocation tests measure the response of the airways to various stimuli, such as methacholine or histamine (American Thoracic Society, 2019).

The treatment of asthma typically involves a combination of pharmacological and non-pharmacological interventions, including inhaled corticosteroids, bronchodilators, and lifestyle modifications, such as avoiding triggers and maintaining a healthy weight (Holgate, 2017). Inhaled corticosteroids are the most effective anti-inflammatory medication for asthma, and are recommended as the first-line treatment for persistent asthma (Global Initiative for Asthma, 2020). Bronchodilators, such as beta-agonists and anticholinergics, can provide quick relief of symptoms, but should not be used as the sole treatment for asthma (American Thoracic Society, 2019).

In addition to these interventions, there are several other treatments that can be used to manage asthma. These include asthma action plans, which can help individuals manage their asthma and prevent exacerbations (National Asthma Education and Prevention Program, 2020). Immunotherapy, which involves the use of allergy shots or sublingual immunotherapy to desensitize the body to specific allergens, can also be effective in reducing symptoms and improving quality of life (Cookson, 2018). Bronchial thermoplasty is a procedure that uses heat to reduce the thickness of the airway walls and improve lung function (American Thoracic Society, 2019).

Overall, asthma is a complex and multifactorial disease that requires a comprehensive approach to management. By understanding the underlying mechanisms of the disease, and using a

combination of pharmacological and non-pharmacological interventions, individuals with asthma can effectively manage their symptoms and improve their quality of life.

Additionally, there are several new and emerging treatments for asthma that are being developed, including biologics, such as monoclonal antibodies, and small molecule therapies (Barnes, 2018). Biologics, such as omalizumab and mepolizumab, have been shown to be effective in reducing symptoms and improving quality of life in individuals with severe asthma (Holgate, 2017). Small molecule therapies, such as tyrosine kinase inhibitors, are also being developed and have shown promise in reducing inflammation and improving lung function (Cookson, 2018).

In conclusion, asthma is a complex and multifactorial disease that requires a comprehensive approach to management. By understanding the underlying mechanisms of the disease, and using a combination of pharmacological and non-pharmacological interventions, individuals with asthma can effectively manage their symptoms and improve their quality of life. New and emerging treatments, such as biologics and small molecule therapies, offer hope for improved management and treatment of asthma in the future.

1.5 REDUCED GLUTATHIONE (GSH)

Reduced glutathione (GSH) is a tripeptide molecule composed of glutamic acid, cysteine, and glycine, and is one of the most important antioxidants in the body (Meister, 1994). It plays a crucial role in maintaining cellular redox balance, protecting cells from oxidative stress, and regulating various cellular processes such as cell growth, differentiation, and survival (Kleinman, 2017). However, reduced glutathione levels have been found to be decreased in various diseases and conditions, including cancer, neurodegenerative diseases, and respiratory diseases (Townsend, 2003). For example, studies have shown that reduced glutathione levels are decreased in patients with chronic obstructive pulmonary disease (COPD), which is a

progressive lung disease characterized by chronic inflammation and oxidative stress (Rahman, 2012). Similarly, reduced glutathione levels have been found to be decreased in patients with asthma, which is a chronic inflammatory disease of the airways (Kirkham, 2013).

The decrease in reduced glutathione levels in these diseases and conditions can be attributed to various factors, including increased oxidative stress, inflammation, and environmental toxins (Forman, 2010). Oxidative stress occurs when the body's antioxidant defenses are overwhelmed by reactive oxygen species (ROS), which can damage cellular components such as DNA, proteins, and lipids (Halliwell, 2007). Inflammation is also a major contributor to decreased reduced glutathione levels, as it can lead to the activation of various inflammatory cells and the release of pro-inflammatory cytokines, which can deplete glutathione levels (Kleinman, 2017). Environmental toxins, such as air pollution and pesticides, can also decrease reduced glutathione levels by inducing oxidative stress and inflammation (Liu, 2018).

The consequences of decreased reduced glutathione levels can be severe, including increased oxidative stress, inflammation, and tissue damage (Townsend, 2003). For example, decreased reduced glutathione levels have been linked to increased oxidative stress and inflammation in the lungs, which can contribute to the development and progression of respiratory diseases such as COPD and asthma (Rahman, 2012). Similarly, decreased reduced glutathione levels have been linked to increased oxidative stress and inflammation in the brain, which can contribute to the development and progression of neurodegenerative diseases such as Alzheimer's and Parkinson's (Kleinman, 2017).

Reduced glutathione levels play a crucial role in maintaining cellular redox balance and protecting cells from oxidative stress and inflammation. However, decreased reduced glutathione

levels have been found in various diseases and conditions, including cancer, neurodegenerative diseases, and respiratory diseases. The decrease in reduced glutathione levels can be attributed to various factors, including increased oxidative stress, inflammation, and environmental toxins. The consequences of decreased reduced glutathione levels can be severe, including increased oxidative stress, inflammation, and tissue damage. Therefore, it is essential to maintain adequate reduced glutathione levels through a balanced diet, supplements, and lifestyle modifications to prevent and treat various diseases and conditions.

1.6 MALONDIALDEHYDE (MDA)

Malondialdehyde (MDA) is a naturally occurring compound that is produced as a byproduct of lipid peroxidation, which is a process in which free radicals attack lipids in cell membranes, resulting in the formation of reactive aldehydes (Esterbauer et al., 1991). The formation of MDA is a complex process that involves the interaction of multiple cellular components, including lipids, proteins, and enzymes (Halliwell & Gutteridge, 2007). The level of MDA in the body is often used as a marker of oxidative stress and lipid peroxidation, and elevated levels of MDA have been linked to a variety of diseases and conditions, including cancer, atherosclerosis, and neurodegenerative disorders (Kehrer & Smith, 1994).

The measurement of MDA levels in the body is often used as a diagnostic tool to assess the level of oxidative stress and lipid peroxidation (Halliwell & Gutteridge, 2007). There are several methods that can be used to measure MDA levels, including spectrophotometry, high-performance liquid chromatography (HPLC), and enzyme-linked immunosorbent assay (ELISA) (Kehrer & Smith, 1994). Each of these methods has its own advantages and disadvantages, and the choice of method will depend on the specific application and the level of sensitivity required (Esterbauer et al., 1991). For example, spectrophotometry is a simple and rapid method that can

be used to measure MDA levels, but it may not be as sensitive as other methods (Halliwell & Gutteridge, 2007).

Elevated levels of MDA have been linked to a variety of diseases and conditions, including cancer, atherosclerosis, and neurodegenerative disorders (Kehrer & Smith, 1994). For example, studies have shown that MDA levels are elevated in patients with cancer, particularly in those with advanced disease (Halliwell & Gutteridge, 2007). Similarly, MDA levels have been shown to be elevated in patients with atherosclerosis, which is a condition characterized by the buildup of plaque in the arteries (Esterbauer et al., 1991). In addition, MDA levels have been linked to neurodegenerative disorders, such as Alzheimer's disease and Parkinson's disease, which are characterized by the progressive loss of neuronal function (Kehrer & Smith, 1994).

The mechanisms by which MDA contributes to disease are complex and multifaceted (Halliwell & Gutteridge, 2007). MDA can react with proteins, DNA, and other cellular components, leading to the formation of advanced lipoxidation end-products (ALEs), which are highly reactive and can cause cellular damage (Esterbauer et al., 1991). MDA can also activate various signaling pathways, including the NF-κB pathway, which can lead to the production of pro-inflammatory cytokines and the promotion of inflammation (Kehrer & Smith, 1994). In addition, MDA can disrupt the function of cellular membranes, leading to changes in membrane fluidity and permeability (Halliwell & Gutteridge, 2007).

In conclusion, malondialdehyde (MDA) is a highly reactive molecule that is produced as a byproduct of lipid peroxidation, and is often used as a marker of oxidative stress and lipid peroxidation. The level of MDA in the body can be measured using a variety of methods, including spectrophotometry, HPLC, and ELISA. Elevated levels of MDA have been linked to a variety of diseases and conditions, including cancer, atherosclerosis, and neurodegenerative

disorders. The mechanisms by which MDA contributes to disease are complex and multifaceted, and involve the reaction of MDA with proteins, DNA, and other cellular components, as well as the activation of various signaling pathways.

CHAPTER TWO

MATERIALS AND METHODS

2.1 PLANT MATERIALS

Synclisia scabrida (meirs) were purchased from Lagos Street in New Benin market, Ring road Benin City, Edo State.

2.2 APPARATUS/EQUIPTMENT

Bench-top centrifuge (Techmel and Techmel, USA), Spectrophotometer (Search Tech 721G Visible Spectrophotometer), Water bath (Techmel and Techmel TT42D, USA)**,** Weighing Balance (Atom-A110C, China)**,** Micropipettes [200ụl and 1000ụl (Sigma USA)]**, ,** 500ml conical flask (Pyrex England)**,** Micropipette (Sigma USA)**,** Conical Flasks (Technico, India)**,** Beakers (Pyrex, USA), Syringes (2.5ml and 5ml)**,** Hand gloves**,** Nose mask**,** Cotton wool**,** Gavage**,** Cages**,** Dissecting kit**,** Ceramic plates**,** Muslin Cloth, Aluminium foil, Glass rod, Measuring cylinder, pH meter, Separating funnel, Glass jar, Retort stand, Lancet mortar and pestle, Testubes, Blade, Scissors, Cuvette, , Masking tape, , Test tubes racks, Drug sachets,Plain bottles, Ethylene Diaminetetracetic Acid (EDTA) sample bottles.

2.3 CHEMICALS AND REAGENTS

Chloroform (Sigma-JHD, Germany), 0.9% Saline solution, distilled water ovalbumin, Aluminium Hydroxide Al $(OH)_3$, Ethanol, stock solution.

2.4 METHODS

2.4.1 Measurement of Body Weights

Body weight was determined using the method of Tonyushkina and Nichols, (1983) as described in the weighing balance manual. The weight of each wistar rats were measured before and after the 14 days treatment period. This was done to ascertain and monitor changes in body weight.

2.4.2 Preparation of Plant Sample

The plant root was used for the experiment. After being collected, it was thoroughly washed with clean water and grinded. The plant powder was dissolved in ethanol and was soaked for 72 hours. Then the mixture is filtered with cheese cloth to yield the extract. The filtrated extract was then transferred to soxhlet extractor to separate the solvent from the extract. The wet extract was dried in a dessicator for 48 hours to yield the dry extract.

A stock solution (80mg/200ml) was prepared by dissolving 40g of extract in 200ml of distilled water from which the volume of plant extract in ml to be administered was collected daily.

2.5 EXPERIMENTAL ANIMAL MODEL AND RESEARCH DESIGN

Twenty(20) female rats weighing between 144-200g were purchased and acclimatized for 21 days .They were fed on pellets and water.They were weighed and distributed into five (3)sub groups in galvanized (containing 5 rats each) 4 rats were given to Pharmacy Students and with a mortality rate of 1. They were injected with 0.5ml of ovalbumin induced asthma every Mondays for three weeks and then administration of the extract at 0.4mL.Daily for 14days of the treatment regime with gavage.The animals were given feed early hours of the day 10-11am and the feed was replaced in the evenings (3pm-4pm). The animals were given free access to drinking water. The cages were cleaned and washed regularly through out the experiment.

Group 1: Control group

This serves as the normal control group .This group was given drinking water and feeds.

Group 2:

This group of rats were induced with ovalbumin but no treatment with synclisia scabrida (meirs) extract

Group 3:

The group of rats were induced with ovalbumin and treated with synclisia scabrida (meirs) extract

2.6 ANIMAL SACRIFICE AND SAMPLE COLLECTION

The animals were handled according to the guidelines of the treatment of laboratory animals by the National Academy Science and published by the National Institute of Health (USA). The ethic regulations have been followed in accordance with national and institutional guidelines for the protection of animals' welfare during experiments. The rats were sacrificed after the treatment regimen. Each rat was anaesthetized by being put in a chloroform saturation chamber. While under chloroform anesthesia the thoracic and abdominal regions were cut open with dissecting tools, blood samples were obtained by cardiac puncture using a 5mL syringe. The blood samples were stored in EDTA bottles and plain bottles labeled. The organs were harvested, washed with normal saline and weighed. Each of the organs were collected and were stored in labeled drug bags and kept in ice. The part of the organs that were stored inside the universal bottles was added formaldehyde to prevent decay.

2.7 PREPARATION OF LUNGS TISSUE

After the experimental period, the Wistar rats were humanely sacrificed, and their lungs were immediately removed and weighed. The lungs were then rinsed with cold phosphate-buffered saline (PBS) to remove any blood or debris. The lung tissue was homogenized in a suitable buffer (e.g., PBS or Tris-HCl) using a tissue homogenizer or sonicator.

The homogenate was then centrifuged to separate the supernatant, which was used for further analysis. The prepared lung tissue sections and homogenates were stored at -80°C or -20°C.

2.8 BIOCHEMICAL ASSAYS

2.8.1 Estimation of Reduced Glutathione (GSH)

The plasma concentration of reduced glutathione (GSH) was determined using the method described by Ellman (1959).

Reagents

5, 5^1-dithiobis-2-nitrobenzoic acid (DTNB), Sodium citrate, Trichloroacetic acid (TCA)

Procedure

To 1.0ml of plasma, 2.5ml 10% of trichloroacetic acid (TCA) was added and centrifuged at 3000rmp for 10mins. 1.0ml of the supernatant was treated with 0.5ml of Ellman's reagent (0.0189% DTNB and 1% sodium citrate) and 3.0ml of 0.3M phosphate buffer (pH 8.0). The yellow colour of the mixture developed was read immediately 412nm and expressed as μM GSH/g plasma.

Calculation

$$\text{GSH concentration} = \frac{A_{test}}{A_{std}} \times C_{std}$$

Where A_{test} = Absorbance of sample

A_{std} = Absorbance of standard

Cstd = Concentration of standard

Calculation of % GSH (Reduced Glutathione) Concentration

Percentage of GSH (% GSH) = (GSH concentration / Total glutathione concentration) × 100

Redox Status = GSH/GSSG

2.8.2 Estimation of Glutathione Peroxidase Activity

Glutathione peroxidase (GPx) activity was measured according to the method described by Nyman(1959).

Principle:

This is based on the oxidation of pyrogallol to purpuragallin by peroxidase, resulting to a deep brown colouration, which is read at 430nm.

Reagent Preparation

Pyrogallol (20mM): 0.2552g of pyrogallol was dissolved in 100ml of distilled water.

Procedure

To an aliquot of homogenate (0.2ml), 2.5ml of phosphate buffer, 2.5ml of H_2O_2 and 1.5ml of pyrogallol were added. The reaction was allowed to stand for 30mins at room temperature. A deep colour was formed, which was read at 430nm.

Calculation

$$\text{Enzyme activity} = \frac{OD/min \times vtDf}{E \times Vs \times Y}$$

Where OD = Absorbance of test

Vt = Total volume of reaction mixture

Df = Dilution factor

E = Molar extinction coefficient (12/M/cm)

Vs = Volume of sample

Y = mg of protein used

2.8.3 Determination of Malondialdehyde (MDA)

Malonaldehyde was determined using the thiobarbituric acid assay (Buege and Aust, 1978)

Principle

Malonaldehyde which is a product of lipid peroxidation react with thiobabituric acid (TBA) to give a red species.

Procedure

A volume of plasma (1.0ml) was added to 2.0ml of TCA-TBA-HCL and mixed thoroughly. The solution was heated for 15mins in a boiling water bath. After cooling, the flocculent precipitate was removed by centrifuged at 1000g for 10min. The absorbance was determined using the formula;

$$\text{MDA (mol/mg protein)} = \frac{A \times V \times 100}{M \times V \times Y}$$

A= Absorbance

V= Total volume of reaction mixture

M= Molar extinction coefficient

V= volume of the sample

Y= mg protein

2.9 STATISTICAL ANALYSIS

The results are presented as mean ± SEM. They were analyzed statistically using Analysis of Variance test (ANOVA) SPSS version 17 and the significance of differences between mean values was determined using least square difference (LSD). They were considered significant at p–value < 0.05.

CHAPTER THREE

RESULTS

The descriptive statistics for glutathione (GSH) and malondialdehyde (MDA) levels across the three groups was shown in Table 1. It revealed important trends related to oxidative stress and the potential protective effects of *Synclisia scabrida* Meirs. The control group (Group 1) had the lowest mean GSH (1.30 ± 0.16 µg/g Prot), while the asthma-induced group without treatment (Group 2) exhibited a significantly higher mean GSH level (1.70 ± 0.25 µg/g Prot). This increase suggests a compensatory antioxidant response to oxidative stress in asthmatic conditions. The treatment group (Group 3), which received *S. scabrida*, showed a reduction in GSH levels (1.43 ± 0.19 µg/g Prot), bringing it closer to control values, suggesting a regulatory effect of the treatment on oxidative stress.

Similarly, MDA levels were highest in Group 2 (1.18 ± 0.37 mol/g Prot), indicating significant lipid peroxidation due to oxidative stress. The control group had lower MDA levels (0.84 ± 0.25 mol/g Prot), while the *S. scabrida*-treated group (Group 3) had the lowest mean MDA level (0.48 ± 0.33 mol/g Prot). The substantial reduction in MDA following treatment suggests a potent antioxidant effect of *S. scabrida* in mitigating lipid peroxidation and oxidative damage in lung tissue.

Figure 1 shows the graphical representation of mean GSH and MDA levels. It further supports the trends observed in the descriptive statistics. The highest GSH levels were observed in Group 2, reinforcing the hypothesis that asthma induces an oxidative stress response. Conversely, MDA levels peaked in Group 2, confirming the presence of oxidative damage. The *S. scabrida* treatment in Group 3 resulted in a downward shift in both markers, aligning closer to the control values, indicating a restoration of oxidative balance.

Statistical comparison of mean GSH levels among the groups was shown in Table 2 and it revealed a significant difference ($p = 0.027$). The untreated asthma group (Group 2) had significantly higher GSH levels than both the control and treatment groups. The reduction in GSH levels following *S. scabrida* treatment suggests that the extract modulated oxidative stress, preventing excessive antioxidant depletion or overcompensation.

The comparison of MDA levels (Table 3) also demonstrated a significant difference among the groups ($p = 0.016$). The highest MDA levels were found in the untreated asthma group (Group 2), while the lowest values were recorded in the *S. scabrida*-treated group (Group 3). The significant reduction in MDA levels following treatment strongly supports the antioxidant potential of *S. scabrida* in counteracting lipid peroxidation, a key marker of oxidative stress in asthma.

Table 4 showed the correlation analysis between GSH and MDA levels. It revealed a significant positive correlation ($r = 0.612$, $p = 0.015$), indicating that as oxidative stress increases (reflected by higher MDA levels), the antioxidant response (GSH levels) also rises. This correlation suggests that *S. scabrida* plays a dual role by lowering oxidative damage (MDA) while stabilizing antioxidant defenses (GSH).

Table 3.1. Descriptive Statistics Glutathione and Malondialdehyde levels

	Glutathione (µ/g Prot)		Malondialdehyde (mol/g Prot)	
	Mean ± SD	Min-Max	Mean ± SD	Min-Max
Group 1	1.30 ± 0.16	1.11-1.55	0.84 ± 0.25	0.47-1.07
Group 2	1.70 ± 0.25	1.42-1.99	1.18 ± 0.37	0.64-1.57
Group 3	1.43 ± 0.19	1.20-1.64	0.48 ± 0.33	0.26-1.07

Key: Group 1: Control

Group 2: Ovalbumin induced asthma no treatment

Group 3: Ovalbumin induced asthma treated with *Synclisia scabrida* Meirs

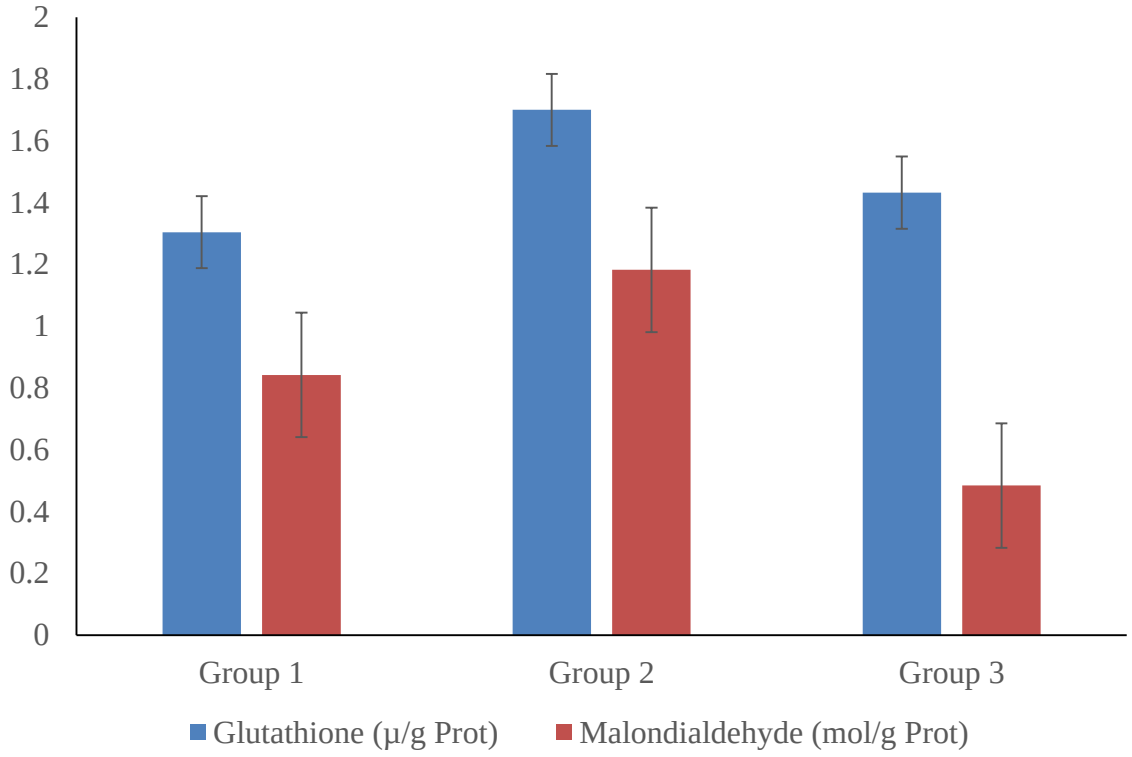

Fig. 3.1. Mean Glutathione and Malondialdehyde values across the various groups

Table 3.2. Comparison of mean Glutathione levels

	Group 1	Group 2	Group 3	p-value
Glutathione (µ/g Prot)	1.304	1.700	1.432	0.027

Key: Group 1: Control

Group 2: Ovalbumin induced asthma no treatment

Group 3: Ovalbumin induced asthma treated with *Synclisia scabrida* Meirs

Table 3.3. Comparison of mean Malondialdehyde (mol/g Prot) levels

	Group 1	Group 2	Group 3	p-value
Malondialdehyde (mol/g Prot)	0.842	1.182	0.484	0.016

Key: Group 1: Control

Group 2: Ovalbumin induced asthma no treatment

Group 3: Ovalbumin induced asthma treated with *Synclisia scabrida* Meirs

Table 3.4. The anti-inflammatory and antioxidant effects of *Synclisia scabrida* Meirs

Glutathione (µ/g Prot)	Malondialdehyde (mol/g Prot)	Correlation (r)	p-value
1.304	0.842	0.612*	0.015
1.7	1.182		
1.432	0.484		

* Correlation is significant at the 0.05 level.

CHAPTER FOUR

DISCUSSION

Oxidative stress plays a crucial role in the pathophysiology of asthma, and glutathione (GSH) is one of the key antioxidants involved in neutralizing reactive oxygen species (ROS) in lung tissues. The present study evaluated the effect of ***Synclisia scabrida*** Meirs on GSH levels in the lung tissue of Wistar rats with ovalbumin-induced asthma. The results revealed that GSH levels were significantly elevated in the untreated asthma group compared to the control group. However, treatment with ***S. scabrida*** led to a reduction in GSH levels, suggesting a modulatory effect on oxidative stress.

The descriptive statistics show that the mean GSH level in the control group was 1.30 ± 0.16 µg/g Prot, while the ovalbumin-induced asthma group without treatment exhibited a significantly higher mean GSH level (1.70 ± 0.25 µg/g Prot). This increase is consistent with findings from Fitzpatrick et al. (2011), who reported that elevated GSH levels in asthma models reflect a compensatory response to oxidative stress. In asthmatic conditions, the excessive production of ROS leads to an upregulation of antioxidant defenses, including GSH synthesis, as a protective mechanism against oxidative damage (Jedli et al., 2022). However, prolonged oxidative stress can overwhelm the antioxidant system, leading to functional impairment of airway macrophages and increased susceptibility to inflammation (Fitzpatrick et al., 2011).

Following treatment with ***S. scabrida***, GSH levels were significantly reduced to 1.43 ± 0.19 µg/g Prot, suggesting that the extract plays a role in stabilizing antioxidant defenses. This reduction aligns with research on other medicinal plants, such as ***Zingiber officinale*** (Jedli et al., 2022) and ***Nasturtium officinale*** (Shakerinasab et al., 2022), which have been shown to restore GSH balance in asthma models. The observed effect of ***S. scabrida*** suggests that it may help regulate oxidative

stress by preventing excessive GSH depletion while also reducing the need for an overcompensatory antioxidant response.

Previous studies have highlighted the dual role of GSH in asthma. While GSH is essential for neutralizing free radicals and reducing oxidative stress, its excessive accumulation may indicate ongoing oxidative damage and increased cellular stress (Rajizadeh et al., 2019). In this study, the elevation of GSH in the untreated asthma group reflects an attempt by lung tissue to counteract oxidative damage. However, the significant reduction in GSH following **S. scabrida** treatment suggests that the extract effectively mitigates oxidative stress, reducing the need for excessive antioxidant compensation.

These findings align with studies on other phytochemicals such as ***Curcumin*** (Shakeri & Boskabady, 2017) and ***Carvacrol*** (Ezz-Eldin et al., 2020), which have demonstrated antioxidant properties by modulating GSH levels in asthma models. The ability of ***S. scabrida*** to regulate GSH levels suggests that it may enhance cellular antioxidant mechanisms while preventing oxidative damage, making it a promising candidate for managing asthma-related oxidative stress.

The study demonstrates that ***Synclisia scabrida*** Meirs has a significant impact on GSH levels in the lung tissue of Wistar rats with ovalbumin-induced asthma. By reducing excessive GSH accumulation, ***S. scabrida*** appears to restore oxidative balance, thereby preventing potential oxidative damage. These findings support the potential of ***S. scabrida*** as an adjunct therapy for managing oxidative stress in asthma.

Malondialdehyde (MDA) is a key biomarker of lipid peroxidation, indicating the extent of oxidative damage in tissues. Elevated MDA levels suggest increased oxidative stress, a hallmark of asthma pathology. This study investigated the impact of ***Synclisia scabrida*** Meirs on MDA levels in the lung tissue of Wistar rats with ovalbumin-induced asthma. The findings showed a

significant increase in MDA levels in the untreated asthma group, while treatment with ***S. scabrida*** resulted in a notable reduction, indicating its potential antioxidant effects.

The descriptive statistics revealed that the mean MDA level in the control group was 0.84 ± 0.25 mol/g Prot, while the ovalbumin-induced asthma group without treatment exhibited a significantly higher mean MDA level (1.18 ± 0.37 mol/g Prot). This sharp increase is consistent with previous research indicating that oxidative stress contributes to lipid peroxidation, damaging lung cell membranes and exacerbating inflammation (Abdel-Fattah et al., 2022). The rise in MDA levels in the untreated asthma group confirms the role of oxidative stress in asthma pathophysiology, aligning with studies by Xue et al. (2016), which reported increased lipid peroxidation in asthmatic models.

Following treatment with ***S. scabrida***, MDA levels significantly decreased to 0.48 ± 0.33 mol/g Prot, suggesting that the extract plays a role in protecting lung tissues from oxidative damage. This reduction aligns with findings from studies on ***Urtica dioica*** (Zemmouri et al., 2017) and ***Echinochrome*** (Abdelmawgood et al., 2024), both of which demonstrated the ability to attenuate lipid peroxidation and oxidative damage in lung tissues. The significant drop in MDA levels suggests that ***S. scabrida*** acts as an effective antioxidant, neutralizing free radicals and preventing lipid membrane oxidation in lung tissues.

Previous studies have established that excessive ROS production in asthma leads to oxidative damage, increasing MDA levels and contributing to airway inflammation and remodeling (Mukherjee et al., 2017). This is particularly concerning as lipid peroxidation products like MDA can exacerbate airway hyperresponsiveness and impair lung function (Rajizadeh et al., 2019). The ability of ***S. scabrida*** to significantly lower MDA levels suggests that it may help prevent these harmful effects, improving lung function and reducing inflammation.

The observed antioxidant effect of ***S. scabrida*** is comparable to that of other natural compounds such as ***Carvacrol*** (Ezz-Eldin et al., 2020) and ***Tyrosol*** (Cellat et al., 2021), which have shown similar reductions in MDA levels in asthma models. These studies highlight the potential of plant-based antioxidants in counteracting oxidative damage and reducing lipid peroxidation in the lungs.

In conclusion, the study findings demonstrate that ***Synclisia scabrida*** Meirs significantly reduces MDA levels in lung tissue, indicating its strong antioxidant capacity. By lowering lipid peroxidation, ***S. scabrida*** may help mitigate oxidative damage, reduce airway inflammation, and improve lung function in asthma. These findings suggest that ***S. scabrida*** could serve as a potential natural therapeutic agent for managing oxidative stress in asthma. Further studies are needed to elucidate the exact mechanisms of action and explore its clinical applicability in asthma management.

Asthma is characterized by chronic airway inflammation and oxidative stress, leading to airway remodeling, hyperresponsiveness, and compromised lung function. The present study examined the anti-inflammatory and antioxidant effects of ***Synclisia scabrida*** Meirs in an ovalbumin-induced asthma model in Wistar rats. The findings demonstrate that ***S. scabrida*** plays a dual role in reducing oxidative stress and inflammation by modulating glutathione (GSH) and malondialdehyde (MDA) levels, two key biomarkers of oxidative damage and antioxidant defense.

A significant positive correlation was observed between GSH and MDA levels ($r = 0.612$, $p = 0.015$), indicating that oxidative stress directly impacts antioxidant responses in asthmatic conditions. Elevated oxidative stress, reflected in the high MDA levels in the untreated asthma group (1.18 ± 0.37 mol/g Prot), suggests an increase in lipid peroxidation and cellular damage.

Similarly, increased GSH levels in the untreated asthma group (1.70 ± 0.25 µg/g Prot) indicate a compensatory response to counteract oxidative stress. However, treatment with ***S. scabrida*** led to a significant reduction in both markers, suggesting that it helps restore oxidative balance.

The anti-inflammatory effects of ***S. scabrida*** are supported by its ability to lower MDA levels (0.48 ± 0.33 mol/g Prot) while maintaining GSH at a regulated level (1.43 ± 0.19 µg/g Prot). These findings align with previous research on natural compounds such as ***Carvacrol*** (Ezz-Eldin et al., 2020) and ***Curcumin*** (Shakeri & Boskabady, 2017), which have been shown to reduce inflammation by inhibiting oxidative stress pathways. Several studies have demonstrated that antioxidants not only scavenge free radicals but also modulate inflammatory pathways, thereby reducing airway inflammation in asthma (Rajizadeh et al., 2019).

Inflammatory mediators such as tumor necrosis factor-alpha (TNF-α) and interleukins play a crucial role in asthma pathophysiology. Studies have shown that plant-derived antioxidants suppress pro-inflammatory cytokines while enhancing the activity of anti-inflammatory mediators (Xue et al., 2016). The significant reduction in oxidative stress markers in the ***S. scabrida***-treated group suggests that the extract exerts anti-inflammatory effects by preventing oxidative damage, which is a major driver of inflammatory responses in asthma.

The findings are further supported by studies on ***Urtica dioica*** (Zemmouri et al., 2017) and ***Echinochrome*** (Abdelmawgood et al., 2024), which showed similar reductions in oxidative stress and inflammation in asthmatic lung tissues. These studies highlight the potential of plant-based antioxidants in mitigating airway inflammation and improving respiratory health.

Overall, the results suggest that ***Synclisia scabrida*** Meirs has significant anti-inflammatory and antioxidant properties in ovalbumin-induced asthma. By reducing lipid peroxidation, stabilizing antioxidant defenses, and potentially modulating inflammatory pathways, ***S. scabrida*** emerges as

a promising therapeutic candidate for asthma management. Further research is needed to investigate its mechanisms of action at the molecular level, particularly its influence on inflammatory cytokines and oxidative stress signaling pathways. Additionally, clinical studies will be necessary to validate its efficacy in human asthma management and explore its potential as a complementary therapy alongside conventional treatments.

CONCLUSION

This study demonstrated that *Synclisia scabrida* Meirs has significant antioxidant and anti-inflammatory effects in an ovalbumin-induced asthma model. Treatment with *S. scabrida* reduced elevated levels of gluthatione (GSH) levels, suggesting a regulatory effect on oxidative stress, while also significantly lowering malondialdehyde (MDA) levels, indicating reduced lipid peroxidation and cellular damage. The strong correlation between GSH and MDA further highlight the extract's role in restoring oxidative balance. By mitigating oxidative stress, *S. scabrida* may also help suppress airway inflammation, supporting its potential as a natural therapeutic agent for asthma management. Future studies should explore its molecular mechanism and clinical applicability to confirm its efficacy and safety for human use.

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