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Anti-Asthmatic Drugs

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Abstract

Asthma is a common seditious complaint that has wide clinical characteristics of the airway of the lungs. Asthma symptoms can be averted by avoiding triggers like allergens and by effective gobbled treatment almost cases with asthma can be duly managed with current drugs. Asthma-related deaths are seen especially in the severe asthma group. Asthma is a miscellaneous complaint, conforming to different phenotypes. It requires a multidisciplinary approach to treatment operation. Severe asthma may suddenly develop in early time in complaint or overtime. There has been substantiation linking age, inflammation, genetics, terrain, and length of illness to severe asthma. The remedy of severe asthma may be told by both environmental and heritable variables.Some traditional shops with Antiasthamatic exertion are Aerva lanta Linn (Amaranthaceae), Ageratum conyzoides, Asystasia gangetica (Acanthaceae), Ficus bengalensis Linn(Moraceae), Piper betel Linn, Argemone Mexicana Linn (Papaveraceous), Datura stramonium Linn(Solanaceae).

Keywords*: Asthma, Epidemiology, Pathophysiology, Risk factors, Antiasthamatic drugs.*

INTRODUCTION

The word "asthma" comes from the Greek word meaning panting or short-drawn breath. The ancient Hebrew literature hasreferred to the condition(1).One of the most prevalent major non-communicable diseases, asthma significantly lowers the quality of life for many people. By disability-adjusted life years, asthma ranks 16th globally among the primary causes of

years lived with disability and 28th among the leading causes of disease burden. Approximately 300 million individuals globally suffer from asthma, and an additional 100 million will probably be impacted by 2025(2).

The most prevalent chronic illness in childhood worldwide, asthma causes a significant amount of morbidity and mortality in children and young people (CYP). Inhalation arises from genetic and environmental variables interacting to cause bronchial inflammation, airway remodeling, and hyperreactivity of the airways. Clinically, this manifests as varying restrictions of airflow and respiratory symptoms such as coughing, wheezing, tightness in the chest, and dyspnea(3).When it comes to sensitization to common inhaled allergens including home dust mites, cockroaches, animal dander, fungus, and pollens, most cases of asthma typically begin in childhood. These allergens that are inhaled promote the proliferation of T helper type 2 (Th2) cells, which in turn promotes the production and release of Th2 cytokines, interleukin (IL)-4, IL-5, and IL-13 (4).

Asthma and COPD are two common and highly burdened chronic airway disorders globally. The majority of patients with COPD and asthma are successfully managed within the main care context by a primary care physician, with practice nurse support as necessary. Referrals to other specialties are made as needed(2). Even with the advancements in asthma therapy over the past few decades, there is room for improvement in patient education, innovative diagnostic techniques, and customized case management(5).

Definition

Asthma is a chronic inflammatory disease of the respiratory system. Airway hyper responsiveness, or an amplification of the airway narrowing reaction to particular triggers including viruses, allergens, and exercise, is linked to chronic inflammation and can result in recurring episodes. Episodes of coughing, chest tightness, wheezing, and/or dyspnea that can change in severity over time. Generally speaking, episodes of symptoms are linked to a broad, changeable restriction of airflow in the lungs, which can usually be reversed either on its own or with the right asthma medication, like a fast-acting bronchodilator (6).

Epidemiology

During the second half of the Twentieth century, notably since the 1960s, a sharp increase in asthma prevalence was observed in several developed countries. This observation was a result of repeated cross-sectional surveys of the prevalence of asthma, mainlyin children but also in adults(5). Asthma is a common chronic illness that affects over 300 million people worldwide. Over the past few decades, it has become more common in many parts of the world, and until recently, it hasbecome more common in developed Western countries on an annual basis(7). Between 1960 and 1985, there was an increase in asthma mortality and hospitalization rates due to acute severe asthma attacks across all age categories, with young preschoolers experiencing the highest rates of growth(5).

Although boys are more likely than girls to have asthma in early childhood, boys also have a higher likelihood of asthma remission during puberty and the early years of adulthood. Furthermore, at this age range, females are more likely than boys to develop asthma. Thus, in adolescence and early adulthood, the sex ratio of asthma during infancy reverses(7).Though a wide variation in prevalence rates has been documented, cross-sectional population-based studies like these, which heavily rely on symptom recognition, may not accurately reflect the true heterogeneity of asthma. Studies of both children and adults have revealed low prevalence rates (2% -4%) in Asian countries (particularly China and India), and high rates (15%–20%) in the United Kingdom, Canada, Australia, New Zealand, and other developed countries (8).

Current epidemiological studies have concentrated on the gut and airway microbiota, prematurity, maternal paracetamol use during pregnancy, and changes in the mother's diet during pregnancy, especially on the levels of micronutrients like omega-3 fatty acids, folate, and vitamin D (the latter two of which modify methylation), and consequently fetal programming (7).It is significant to remember that decreased asthma incidence and/or better asthma control at the community level are what lead to a decrease in the prevalence of current asthma. As a result, a decline in the prevalence of current asthma may accurately represent increasing drug use brought about by more common prescribing practices and improved compliance (5).

Pathophysiology

The pathophysiology of asthma is characterized by several mediators; while symptoms may come and go; the inflammation of the airways remains permanent. Cysteinyl, leukotrienes, chemokines, cytokines (like IL-1β, TNF-α, GM-CSF, IL-4, IL-5, and IL-13), histamine, prostaglandin D2, nitric oxide, and activated mast cells are among the mediators involved in the pathogenesis of asthma. The inflammation that is associated with asthma is mediated by activated mast cells, activated eosinophils, and a rise in the receptors of T helper and natural killer (NK) T cells (9).Allergenic (such as home dust mites, cockroach remnants, animal dander, mold, and pollens) and non-allergic (such as virus infections, tobacco smoke exposure, cold air, and exercise), asthma triggers can set off a series of events that culminate in chronic airway inflammation. Increased T2 cell counts in the airways trigger the release of particular cytokines, such as interleukin (IL)-4, IL-5, IL-9, and IL-13, as well as eosinophilic inflammation and the formation of immunoglobulin E (IgE) (6).

Interaction between T cells and specialized antigen-presenting airway dendritic cells (DCs) is also necessary for allergen sensitization. This technique entails the conversion of allergens into short peptides, which are then selectively presented to naive T cell receptors via the MHC class II major histocompatibility complex. Naive T cells identify the chemicals, and they collaborate with DCs to form an immunological synapse that promotes allergen presentation. After the airways become sensitized, additional exposure to the allergen causes a mast-cell-driven early-type bronchoconstrictor response (EAR), which involves the release of histamine, prostaglandin D2, and leukotriene C4 (LTC4) and lasts for five to ninety minutes (7). The synthesis of IgE in turn sets off the release of inflammatory mediators, including histamine and cysteinyl leukotrienes, which result in edema, increased mucous secretion, and bronchospasm a contraction of the smooth muscle in the airways all of which are hallmark symptoms of asthma(6).

Symptoms (10)

- Wheezing
- Breathlessness
- Difficulty in speaking
- Sputum Production
- Dyspnoea

- Tightness of Neck Muscle
- Coughing after physical activity
- Whistling Sound while breathing
- Frequent coughing
- Grayish or bluish coloring of lips
- Chest Tightness
- Feeling Frightened, exhaustion

RISK FACTORS

Environmental condition

Early exposure to aeroallergens increases a child's risk of developing persistent asthma later in life, compared to their counterparts who do not have this sensitivity. In addition, the onset, severity, and morbidity of asthma are linked to seasonal allergic rhinitis and indoor allergen exposure. Specifically, there is a particularly substantial correlation between dust mite exposure and asthma, with over 50% of children and adolescents with asthma being sensitive to dust mites, compared to typically less than 20% of children without asthma (7).

Viral condition

Childhood viral infections are the most prevalent cause of asthma exacerbations and are linked to the development of asthma. This is notably the case with rhinovirus and RSV infections. RSV is a significant contributor to infantile bronchiolitis and a separate predictor of recurrent wheezing and early-life asthma. Respiratory viral infections, especially those causing wheezing episodes in the first three years of life due to rhinovirus, have been shown in several longitudinal and birth-cohort studies to be good indicators of the development of asthma later on. A comparatively low level of type 1 and type 3 interferon production together with T2-type (7).

Air Pollution

Asthma development and exacerbation are largely caused by indoor and outdoor air pollution, both of which have grown with urbanization and population growth, especially in developing nations. Nitrogen dioxide, ozone, volatile organic compounds, particulate matter, and traffic-related air pollution which includes particulates originating from non-combustion and fresh vehicle exhaust—are the pollutants linked to asthma. These pollutants decrease inhibitory

TReg function and cause oxidative stress and epithelium damage, which either starts or intensifies airway inflammation (7).

Tobacco Smoke

Smoke from tobacco products, which is made up of a complex mixture of nitrogen dioxide and other volatile chemical compounds, is a known risk factor for the development of asthma. It works in part by enhancing T2-type responses. The second generation is more susceptible to asthma due to maternal smoking during pregnancy, which further supports the role of intrauterine epigenetic pathways in the development of asthma(7).

Obesity

Childhood obesity is closely linked to both the prevalence and severity of asthma. Additionally, excessive gestational weight gain and maternal obesity are linked to a higher risk of asthma in children, particularly in mothers who are not asthmatic. These correlations could be explained by a combination of mechanical elements, and common causative metabolic, hormonal, and low-grade inflammatory pathways. For example, elevated levels of inflammatory cytokines (TNF, IL-1, and IL-6) produced by macrophages and adipokines (leptin, chemerin, and adiponectin) produced by adipocytes that impair cell proliferation and damage tissue characterize the obesity-associated chronic inflammatory response. Leptin regulates the production of pulmonary surfactants in the developing lungs of fetuses and acts as a sentinel mediator of lipofibroblast differentiation. Leptin infusion improves airway function in mice (7).

Asthma-related mortality risk factors include (11)

- History of abrupt, severe escalation in the past.
- Previous asthma inhalation.
- Earlier admission to an intensive care unit for asthma.
- At least two asthma-related hospital stays in the previous 12 months.
- At least three asthma-related ER visits over the previous 12 months.
- Hospitalization or an ER visit related to asthma within the last 30 days.
- Using more than two canisters of inhaled short-acting β2-agonist each month
- Systemic corticosteroids are being used now, or they have recently been stopped.
- Having trouble recognizing the extent of an airflow restriction.

- Comorbidities, such as chronic obstructive pulmonary disease or cardiovascular disorders.

DIAGNOSIS (12)

A comprehensive medical history, physical examination, and objective measurements of lung function in children ≥6 years old (spirometry) are all necessary for the diagnosis of asthma. Recommended, to record fluctuating expiratory airflow limitation and validate the diagnosis, both before and following the bronchodilator (6). The most crucial diagnostic technique for determining if a blockage in the airway is reversible is spirometry. It ought to be carried out on every patient for whom asthma is a possible diagnosis (12).

Since viral infections are frequently linked to episodes of wheezing and coughing, diagnosing asthma in children can be more challenging because, in between exacerbations, children may appear asymptomatic during routine physical examinations. Additionally, while spirometry can be done on some children as young as five years old, it is frequently unreliable in patients under the age of six (6). In patients with suspected asthma and normal spirometry, bronchoprovocation with methacholine can be beneficial because a negative test result makes the diagnosis of asthma doubtful (12).

Diagnostic modality	Symptoms	Other differential Features
Clinical History	Wheezing, coughing, chest tightness May only be present or worsened with exertion, upper respiratory infection, seasonal or perennial allergies Nocturnal cough, particularly from 2 AM to 4 AM Need for short-acting B_2-agonist inhaler for relief of symptoms Personal or family history of atopy	Occupational exposure sansadxa Dyspnea only on exertion n may suggest COPD Family history is often positive in atopic asthma Seasonal variation of symptoms or asthma severity is consistent with atopic asthma
Spirometry	Airway obstruction evidenced by FEV, : FVC ratio <lower limit of normal Demonstrated reversibility of	Airflow limitation that is irreversible or partially reversible may suggest

	obstruction by increase in FEV, 2200 mL and ≥12% from baseline measure after inhalation of 2-4 puffs of short-acting ß2-agonist Normal spirometry findings are not inconsistent with asthma	COPD, bronchiectasis, or disease other obstructive
Bronchoprovocation with methacholine	20% or more decrease in FEV, with after inhalation of low concentration (<4 mg/mL) of methacholine; used principally in patients with symptoms consistent with pulmonary function tests asthma but who exhibit normal.	Specificity and positive predictive value are low Allergic rhinitis, congestive heart failure, and chronic bronchitis may all exhibit increased methacholine response
Impendence oscillometry	Elevated airway resistance at 5 Hz, elevated area of reactance, increased resonant frequency, reactance at 5Hz more negative than predicted	Increased total airway resistance at 5 Hz in comparison with large-airway resistance at 20 Hz suggests small-airway disease
Chest radiograph or CT scan of thorax	Usually normal but can exclude other diagnoses such as emphysema, lung cancer, infiltrative diseases, pneumonia	Central bronchiectasis may suggest allergic bronchopulmonary aspergillosis
CBC	Eosinophilia, particularly >300/µL; results can inform selection for mepotizumab or reslizumab therapy	Eosinophilcounts 150 mitigates against use of anti-IL-5 therapies
Serum total IgE	Elevated in atopic asthma, not in nonatopic asthma, can inform the selection of omalizumab therapy	IgE >1000 IU/mL: consider allergic bronchopulmonary aspergillosis, atopic dermatitis, and other allergic manifestations
Skin prick testing or	Positive, particularly for perennial	A positive test for

serum–specific IgE for aeroallergens	allergens, or seasonal allergens with corresponding seasonal variation in asthma symptoms, may be negative in nonatopic asthma, and can inform omalizumab therapy Positive testing can guide allergen avoidance strategies	Aspergillus fumigatus or A niger suggests. possibility of allergic bronchopulmonary aspergillosis
Fractional excretion of nitric oxide	Intermediate level: 25-50 ppb in patients aged ≥12y High level: >50 ppb in patients aged ≥12 y	Low levels are not inconsistent with asthma Levels > 20 may identify omalizumab-responsive patients

DRUGS USED IN ASTHMA TREATMENT

Bronchodilators/Relievers

Sympathomimetic

Moa: When it comes to sympathomimetic drugs, their mechanisms can be either direct (drug and receptor interaction), like α-adrenergic agonists, β-adrenergic agonists, and dopaminergic agonists, or indirect (drug and receptor interaction not between drug and receptor), like release stimulants, COMT inhibitors, MAOIs, and reuptake inhibitors that raise endogenous catecholamine levels (13).

- Salbutamol
- Albuterol
- Terbutaline
- Bambuterol
- Salmeterol
- Formoterol

Methylxanthines

Moa: It does this by inhibiting cyclic nucleotides phosphodiesterase (PDE), which stops cAMP and cGMP from converting to 5'-AMP and 5'-GMP, respectively. PDE inhibition causes cAMP and cGMP to accumulate intracellularly (14).

- Theophylline
- Aminophylline

Anticholinergics

Moa: These medications work by taking up receptor sites at parasympathetic nerve terminals, which reduce the number of receptor sites available for acetylcholine receptor response. The degree of parasympathetic activity and the number of receptors inhibited by anticholinergic medications determine how much parasympathetic response is present or reduced. Anticholinergic medications act on cholinergic muscarinic receptors throughout the body, which causes effects in the heart, brain, smooth muscle, glands, and eyes, among other areas(15).

- Ipratropium bromide
- Tiotropium bromide

Anti- Inflammatory Agents/Controllers

Leukotriene Receptor Antagonists

Moa-inhibits the activity of LTD4 on cys-LT1 receptors on basophils, eosinophils, mast cells, and bronchi(16).

- Montelukast
- Zafirlukast

Mast Cell Stablizers

Moa: Mast cell stabilizers are cromone drugs that are used to treat or avoid specific allergic reactions. By stopping mast cell degranulation, they stabilize the cell and stop histamine and other associated mediators from being released. The inhibition of IgE-regulated calcium channels is one possible pharmacodynamics mechanism. The histamine vesicles are unable to fuse to the cell membrane and degranulate in the absence of intracellular calcium (17).

- Sodium cromoglycate
- Nedocromil
- Ketotifen (5HT action)

Corticosteroid

Systemic

Moa: The corticoreceptor-ligand complex translocates into the cell nucleus upon contact, where it binds to many glucocorticoid response elements (GRE) located in the target genes' promoter region. Following its interaction with fundamental transcription factors, the DNA-

bound receptor modifies the expression of particular target genes, including the production of IL2 (interleukin 2) (18).

- Hydrocortisone
- Prednisolone

Inhalational

Moa: Contact with the corticoreceptor-ligand complex causes it to translocate into the cell nucleus, where it binds to many glucocorticoid response elements (GRE) found in the promoter region of the target gene. After binding to basic transcription factors, the DNA-bound receptor alters the expression of specific target genes, such as the IL2 (interleukin 2) gene (19).

- Beclomethasone dipropionate
- Budesonide
- Fluticasone- propionate
- Flunisolide

Anti –IgE Humanized Monoclonal Antibodies

Moa: (It binds to an antigenic epitope on IgE that overlaps with the location where FcεRI interacts, inhibiting the binding of IgE to FcεRI on mast cells and basophils. Because a normal anti-IgE antibody can cross-link cell surface FcεRI-bound IgE, thereby aggregating FcεRI, and activating mast cells and basophils to release the plethora of chemical mediators contained in the densely packed sacs inside the cells, this property is crucial to its pharmacological effects(20).

- Omalizumab

Some traditional plants with antiasthmatic potential

Aerva lanta Linn (Amaranthaceae)

The common wayside herbaceous weed Aerva Lanta, also known as A. lanta, grows upright or prostrate and is distinguished by small, white, fuzzy blooms borne in axillary bunches along its branches. On the plains in the warmer regions of India, it is widely distributed. Antiasthmatic activity has been shown for an ethanol extract of A. lanata aerial parts at 100 mg/mL in the isolated goat tracheal chain preparation paradigm and 30 and 60 mg/kg oral doses in clonidine-induced catalepsy and mast cell degranulation in mice (21).

Ageratum conyzoides

Ageratum conyzoides, also known as L. Ageratum conyzoides, is an annual herbaceous plant that is native to tropical America and can be found throughout tropical and subtropical regions of the world. It is a member of the Asteraceae (Compositae) family. Mice treated with a hydroalcoholic extract of A. conyzoides leaves at dosages of 250, 500, and 1,000 mg/kg exhibit antihistaminic efficacy by preventing clonidine-induced catalepsy (22).

Asystasia gangetica (Acanthaceae)

In various regions of Nigeria, Asystasia gangetica, often known as A. gangetica, is used to treat asthma. Akah, et al. used guinea pig trachea, rat stomach strips, guinea pig ileal preparation, and egg albumin-induced acute inflammation to assess the antiasthmatic activity of hexane, ethylacetate, and methanol extracts of A. gangetica leaves. The findings showed that while the extracts decreased the contraction induced by spasmogens, they did not show any contractile or relaxing effect in isolated tissue preparations (23).

Ficus bengalensis Linn (Moraceae)

Ficus bengalensisis, also known as F. bengalensis, is a massive tree that grows to a height of around 30 m and has numerous aerial roots that fall from its branches. At a concentration of 50 mg/kg, ethanol, ethyl acetate, and aqueous extracts of F. bengalensis bark, along with fractions extracted from this extract, exhibit antihistaminic activity by preventing mice from developing catalepsy brought on by clonidine. The existence of flavonoids may be the cause of these actions (24).

Piper betel Linn

Lantana camara is one such pantropical weed that is affecting the ecosystem, and causing biodiversity loss to a greater extent. It is a shrub that belongs to the family of Verbenaceae. Plant extracts are used for the treatment of cancers, chicken pox, measles, asthma, ulcers, swellings, eczema, tumors, high blood pressure, bilious fevers, catarrhal infections, tetanus, rheumatism, malaria, and atopy of abdominal viscera(25).

Argemone mexicana Linn (Papaveraceae)

It is considered an important medicinal plant in India. The yellow juice, which exudes when the plant is injured, has found usage as traditional medicine in India for dropsy, jaundice,

ophthalmia, scabies, and cutaneous infections. Its various parts have been used in chronic skin diseases, emetic, expectorant, demulcent, and diuretic, while its seeds and seed oil have been used for the treatment of dysentery, ulcers, asthma, and other intestinal infections(26).

Datura stramonium Linn (Solanaceae)

A member of the Solanaceae family, Datura stramonium grows wild and is commonly accessible around the world. Numerous toxic tropane alkaloids, including atropine, hyoscamine, and scopolamine, are present in them. Ayurveda has been utilized to treat a range of conditions, including sciatica, ulcers, wounds, inflammation, rheumatism, gout, bruising, swellings, fever, asthma, bronchitis, and toothaches(27).

Classification of Anti-Asthmatic Herbs Based on Mechanism of Action (10)

Table 1: Bronchodilators

Sr. No	Name of plant	Part used/extract/fraction	Major chemical constituent(s)
1	Adhatoda vasica Nees	Leaves, Roots	Alkaloids
2	Albizzia lebbeck (Sareesha rakat)	Stem bark /Aqueous	Saponin
3	Alstonia scholaris	Leaves / Ethanol	Ditamine , Echitamine and Echietnines
4	Artemisia caerulescens	Aerial parts of Butanol	Quercetin , isorhamnetin

Table 2: Mast cell stabilizers

Sr. No	Name of plant	Part used/extract/fraction	Major chemical constituent(s)
1	Achyranthes aspera	Aerial parts Bulbs/Juice Aqueous	Oleanolic acid
2	Albizzia lebbeck	Stem bark/Aqueous	Saponins
3	Allium cepa	Bulbs/Juice	α and β unsaturated Thiosulphinates
4	Aquillaria agallocha	Stem/Aqueous extract	Triterpenoids

Table 3: Anti-allergic

Sr. No	Name of plant	Part used/extract/fraction	Major chemical constituent(s)
1	Adhatoda vasica	Leaves/Methanol	Vasicinol, vasicine
2	Albizzia lebbeck	Stem bark/Aqueous	Saponins
3	Alisma orientale	Rhizomes/Aqueous, Methanol	Alisol B monoacetate, Alismaketones-B 23-acetate and –C 23-acetate
4	Aquillariaagallocha	Stem/Aqueous extract	Triterpenoids

Table 4: Anti-inflammatory agents

Sr. No	Name of plant	Part used/extract/fraction	Major chemical constituent(s)
1	Asystasia gangetica	Leaves/Methanol, Ethyl Acetate	Isoflavone glycoside, dalhorinin
2	Aloe vera Tourn. Ex Linn. (Liliaceae)	Leaves/Aqueous, Chloroform and ethanol	Anthraquinones, sterols, saponins, and carbohydrate
3	Bryonia laciniosa	Leaves/chloroform extract	Flavonoids
4	Calotropisprocera	Latex	α-amyrin,β-amyrin calotropin (Triterpenoid)

Table 5: Anti-spasmodic agents

Sr. No	Name of plant	Part used/extract/fraction	Major chemical constituent(s)
1	Aegle marmelos	Leaves/Ethanol	Aegelin, Aegelemine,Aegeline
2	Asiasarum sieboldi	Roots/Methanol	Methyleugenol, gamma asarone, Elemicin, Asarinin

3	Asystasia gangetica	Leaves/Methanol, Ethyl acetate	Isoflavone glycoside, dalhorinin
4	Bacopa monniera	Leaves/Ethanolic	Bacosides, Alkaloids,Glycosides

CONCLUSION

Bronchial asthma is a worldwide common complaint and is characterized by reversible tailwind limitation, with non-specific AHR related to airway inflammation. Asthma is characterized by variable airway inhibition, hyperresponsiveness, and inflammation. Antipathetic respiratory diseases in particular asthma are added in the developed and developing countries and pose a serious global health problem and profitable burden. Numerous cross-sectional studies have verified increases in the prevalence and frequency of asthma over the history of 2 to 3 decades, but much remains unknown as to the abecedarian immunologic, inheritable, and environmental mechanisms underlying the development of this condition and its increased expression, especially in the advanced world. Asthma drug with quick relief drugs for anticholinergic, short-acting gobbled beta2 agonist. In this papermedicines used in asthma with their medium are described, and sauces bracket and advice for taking asthmatic medicine. As from the above explanation, it's easily linked that medicinal shops are estimated and their useful corridor are reported grounded on their effectiveness in bronchial asthma and their explanation also shows their prospective salutary effect of these conditions.

REFERENCES

1. Chronic Disease Follow-Ups for Adults in Primary Care by Karahan S., Page no- 4-6.
2. V.M. McDonald et al. Multidisciplinary care in Chronic Airway Diseases: the Newcastle Model.ERJ Open Res 2022, Vol.8,10 June 2022, Page no- 1-12.
3. Jones H, LawtonA, Gupta A, Asthma Attack in Children - Challenges and Opportunities, IJOP, Vol.89, Issue-4,21 Jan 2022, Page no- 373-377.
4. Kudo et al. Pathology of Asthma, Frontiers in microbiology, Volume-4, Article -263, 10 Sep 2013, Page no -1- 16.
5. Dharmage SC, Perret JL and Custovic A Epidemiology Asthma in Children and Adults, Frontiers in Pediatrics, Vol.7, Article 246,18 June 2019, Page No - 1-15.

6. Quirt et al. Asthma. Allergy Asthma Clinical Immunology, Vol.14(Suppl.2), Issue-50,2018,Page no – 15-30.
7. S Holgate, Asthma, NRDP, Vol.1,2015, Page no -1-22.
8. Padmaja Subbarao, Piush J. Mandhane, Asthma: epidemiology, etiology, and risk factors,CMAJ,Vol.181,Issue-9, 27 Oct 2009,Page no – E181-E190.
9. Seda Beyhan SAĞMEN, Berrin CEYHAN, Severe Asthma, Kocatepe Medical Journal,Vol.19, 1 Feb 2018, Page no – 157-163.
10. Zaseem et al. An Overview on Antiasthamatic Drugs, WJPR, Vol.6, Issue-8, 27 July 2017, Page no – 780-789.
11. Papiris et al. Clinical review: Severe asthma, Critical Care, Vol.6, Issue -1, Feb 2022, Page No – 1-15.
12. Jennifer L. Mc Cracken, et al. Diagnosis and Management of Asthma in Adults, Clinical review and education, Vol.318, Issue-3,11July 2017, Page no 279-290.
13. H. Bönisch, U. Trendelenburg: The mechanism of action of indirectly acting sympathomimetic amines. Handbook Experimental Pharmacol, 1988; 90, Page no-247–277.
14. https://www.slideshare.net/ParasuramanParasuraman/drugs-used-in-bronchial-asthma.
15. https://medipub.blogspot.in/2011/10/anticholinergic-medications-mechanism_24.html.
16. https://www.slideshare.net/talkoncorners2/montelukast-by-aseem.
17. https://en.wikipedia.org/wiki/Mast_cell_stabilizer
18. https://www.drugbank.ca/drugs/DB00860
19. https://www.uptodate.com/contents/molecular-effects-of-inhaled-glucocorticoid-therapy.
20. MacGlashan DW, Bochner BS, Adelman DC, Jardieu PM, Togias A, McKenzie-White J, Sterbinsky SA, Hamilton RG, Lichtenstein LM (February). "Down-regulation of Fc (epsilon) RI expression on human basophils during in vivo treatment of atopic patients with anti-IgE antibody". Journal of Immunology, 1997; 158(3), Page no- 1438–45.
21. Tote M. V., Mahire N. B., Jain A. P., Bose S., Undale V. R., Bhosale A. V. Effect of Ageratum conyzoides Linn on clonidine and haloperidol-induced catalepsy in mice Pharmacologyonline, 2009; 2, Page no- 186-194.
22. Bhalke R. D., Gosavi S. A., Antistress and antiallergic effect of Argemone mexicana stem in asthma, Arch. Pharm Sci Res,2009; 1(1), Page no- 127-129.

23. Akah P. A., Ezike A. C., Nwafor S. V., Okoli C. O., Enwerem N. M. Evaluation of the anti-asthmatic property of Asystasia gangetica leaf extracts. J Ethnopharmacology, 2003; 89, Page no- 25-36.
24. Taur D. J., Patil R. Y. Effect of bio-fractions isolated from Ficus bengalensis bark on clonidine-induced catalepsy. J Pharmacy Research, 2009; 2(11), Page no- 1676-1677.
25. Jawale N. M., Shewale A. B., Nerkar G. S., Patil V.R. Evaluation of antihistaminic activity of leaves of Piper betel Linn. Pharmacologyonline, 2009; 3, Page no- 966-977.
26. Brahmachari G., Gorai D., Roy R. Argemone mexicana: chemical and pharmacological aspects. Revista Brasileira de Farmacognosia. 2013; 23(3), Page no- 559-67.
27. Gaire B. P., Subedi L. A review on the pharmacological and toxicological aspects of Datura stramonium L. Journal of integrative medicine. 2013; 11(2), Page no- 73-9.