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SL .No	Title of paper	Name of the Teacher	Name of journal	Year of publication	ISSN number	Link to the recognition in UGC enlistment of the Journal /Digital Object Identifier (doi) number	
						Link to website of the Journal	Link to article / paper / abstract of the article
1	A CONTEMPORARY OVERVIEW OF PPAR/Γ DUAL AGONISTS FOR THE MANAGEMENT OF DIABETIC DYSLIPIDEMIA	DR. P. Balakumar	CURRENT MOLECULAR PHARMACOLOGY	2018	1874-4672	<a href="https://benthamscience.com/journals/current-molecular-pharmacology">https://benthamscience.com/journals/current-molecular-pharmacology</a>	<a href="https://www.eurekaselect.com/article/95725">https://www.eurekaselect.com/article/95725</a>
2	A CRITICAL REVIEW ON HYPOTHESIS, PATHOPHYSIOLOGY OF SCHIZOPHRENIA, AND ROLE OF VITAMINS IN ITS MANAGEMENT	DR. N. Venkateshwaramurthy	ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH	2018	0974-2441	<a href="https://journals.innovareacademics.in/index.php/ajpcr/index">https://journals.innovareacademics.in/index.php/ajpcr/index</a>	<a href="https://journals.innovareacademics.in/index.php/ajpcr/article/view/23259">https://journals.innovareacademics.in/index.php/ajpcr/article/view/23259</a>
3	A PATHOPHYSIOLOGICAL APPROACH OF MACROVASCULAR COMPLICATION IN DIABETES MELLITUS WITH HYPERTENSION: A SYSTEMATIC REVIEW	DR. R. Shanmuga Sundaram	RESEARCH JOURNAL OF PHARMACY AND TECHNOLOGY	2019	0974-360X (ONLINE) 0974-3618 (PRINT)	<a href="https://www.rjptonline.org/">https://www.rjptonline.org/</a>	<a href="https://www.rjptonline.org/abstractview.aspx?pid=2019-12-2-73">https://www.rjptonline.org/abstractview.aspx?pid=2019-12-2-73</a>



PRINCIPAL

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4	A POTENTIAL ROLE OF THE RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM IN EPITHELIAL-TO-MESENCHYMAL TRANSITION-INDUCED RENAL ABNORMALITIES: MECHANISMS AND THERAPEUTIC IMPLICATIONS	DR. P. Balakumar	PHARMACOLOGICAL RESEARCH	2019	1096-1186	<a href="https://www.sciencedirect.com/science/article/abs/pii/S1043661819307637">https://www.sciencedirect.com/science/article/abs/pii/S1043661819307637</a>
5.	A QUALITATIVE KNOWLEDGE ASSESSMENT OF PREGNANT WOMEN ON PRETERM BIRTH IN A TERTIARY CARE HOSPITAL	DR. N. Venkateshwaramurthy	INTERNATIONAL JOURNAL OF LIFE SCIENCE AND PHARMA RESEARCH	2018	2250-0480	<a href="https://ijlpr.com/index.php/journal/Home">https://ijlpr.com/index.php/journal/Home</a>
6.	A REVIEW ON RELEVANCE OF HERBAL MEDICATIONS FOR PSYCHIATRIC PATIENTS	DR. N. Venkateshwaramurthy	RESEARCH JOURNAL OF PHARMACY AND TECHNOLOGY	2019	0974-360X	<a href="https://www.rjtonline.org/AbstractView.aspx?PID=2019-12-7-6">https://www.rjtonline.org/AbstractView.aspx?PID=2019-12-7-6</a>
7	A REVIEW ON THE EFFECT OF IMMUNOSUPPRESSANTS ON FERTILITY	Mr. T. Thiagarajan	RESEARCH JOURNAL OF PHARMACY AND TECHNOLOGY	2019	0974-360X (ONLINE) 0974-3618 (PRINT)	<a href="https://www.rjtonline.org/abstractview.aspx?pid=2019-12-3-78">https://www.rjtonline.org/abstractview.aspx?pid=2019-12-3-78</a>
8	A REVIEW ON THE IRRATIONAL ANTIBIOTICS USAGE IN PEDIATRICS FOR RESPIRATORY TRACT INFECTIONS	Ms. M. Sudha	RESEARCH JOURNAL OF PHARMACY AND TECHNOLOGY	2019	0974-360X (ONLINE) 0974-3618 (PRINT)	<a href="https://www.rjtonline.org/abstractview.aspx?pid=2019-12-10-98">https://www.rjtonline.org/abstractview.aspx?pid=2019-12-10-98</a>



9	AN OBSERVATIONAL STUDY OF MEDICATION ERRORS AMONG PSYCHIATRIC PATIENTS IN A TERTIARY CARE HOSPITAL	DR. K. Krishnaveni	ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH	2018	2455-3891	<a href="https://journals.innovareacademics.in/index.php/ajpcr/index">https://journals.innovareacademics.in/index.php/ajpcr/index</a>	<a href="https://journals.innovareacademics.in/index.php/ajpcr/article/view/27601">https://journals.innovareacademics.in/index.php/ajpcr/article/view/27601</a>
10	ASSESSMENT ON PREVALENCE OF HYPERTENSION AND ITS ASSOCIATED RISK FACTORS ALONG WITH MMAS SCORE IN A RURAL COMMUNITY: A HOME BASED SCREENING	DR. K. Krishnaveni	ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH	2018	2455-3981	<a href="https://journals.innovareacademics.in/index.php/ajpcr/index">https://journals.innovareacademics.in/index.php/ajpcr/index</a>	<a href="https://journals.innovareacademics.in/index.php/ajpcr/article/view/26473">https://journals.innovareacademics.in/index.php/ajpcr/article/view/26473</a>
11.	IMPACT OF A PHARMACIST INTERVENTION ON IMPROVING MEDICATION ADHERENCE AND KNOWLEDGE TOWARDS DIABETES MELLITUS: A RANDOMISED CONTROLLED STUDY	DR. K. Krishnaveni	INTERNATIONAL JOURNAL OF PHARMACEUTICAL RESEARCH	2019	0975-2366	<a href="http://www.ijpronline.com/">http://www.ijpronline.com/</a>	<a href="http://www.ijpronline.com/viewarticledetail.aspx?id=7424">http://www.ijpronline.com/viewarticledetail.aspx?id=7424</a>
12	MOLECULAR TARGETS OF FENOFIBRATE IN THE CARDIOVASCULAR-RENAL AXIS: A UNIFYING PERSPECTIVE OF ITS PLEIOTROPIC BENEFITS	DR. P. Balakumar	PHARMACOLOGICAL RESEARCH	2019	1096-1186	<a href="https://www.sciencedirect.com/science/article/abs/pii/S1043661819302762">https://www.sciencedirect.com/science/article/abs/pii/S1043661819302762</a>	<a href="https://www.sciencedirect.com/science/article/abs/pii/S1043661819302762">https://www.sciencedirect.com/science/article/abs/pii/S1043661819302762</a>
13.	PHARMACOGENETICS AND GENETIC POLYMORPHISM OF CYP ENZYMES IN INDIAN POPULATION: A CLINICAL	DR. R. Shanmuga Sundaram	RESEARCH JOURNAL OF PHARMACY AND TECHNOLOGY	2018	0974-3618	<a href="https://riptonline.org/home.aspx">https://riptonline.org/home.aspx</a>	<a href="https://riptonline.org/home.aspx?journal=research%20journal%20of%20">https://riptonline.org/home.aspx?journal=research%20journal%20of%</a>



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	REVIEW						20pharmacy%20and%20technology;pid=2018-11-12-78
14.	PHARMACOLOGICALLY RELEVANT DRUG INTERACTIONS OF SULFONYLUREA ANTIDIABETICS WITH COMMON HERBS	DR. B. Rajkapoor	JOURNAL OF HERBMED PHARMACOLOGY	2018	23455004	<a href="http://www.herbmedpharmacol.com/">http://www.herbmedpharmacol.com/</a>	<a href="http://www.herbmedpharmacol.com/article/jhp-1280#:~:text=in%20addition%2c%20the%20antidiabetic%20herbal%20supplements%20such%20as,of%20interacting%20pharmacokinetic%20and%20pharmacodynamically%20with%20sulfonylurea%20antidiabetics">http://www.herbmedpharmacol.com/article/jhp-1280#:~:text=in%20addition%2c%20the%20antidiabetic%20herbal%20supplements%20such%20as,of%20interacting%20pharmacokinetic%20and%20pharmacodynamically%20with%20sulfonylurea%20antidiabetics</a>
15.	REVIEW ON CLINICALLY DEVELOPING ANTIBIOTICS	DR. R. Sambathkumar	INTERNATIONAL JOURNAL OF APPLIED PHARMACEUTICS	2018	0975 7058	<a href="https://journals.innovareacademics.in/index.php/ijap/article/view/22668/14665">https://journals.innovareacademics.in/index.php/ijap/article/view/22668/14665</a>	<a href="https://journals.innovareacademics.in/index.php/ijap/article/view/22668/14665">https://journals.innovareacademics.in/index.php/ijap/article/view/22668/14665</a>
16.	ROLE OF CHLOROQUINE AS AN ANTICANCER AGENT	Ms. M. Sudha	INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACEUTICAL SCIENCES	2018	9757538	<a href="https://iirps.com/index.php/home/article/view/4199">https://iirps.com/index.php/home/article/view/4199</a>	<a href="https://iirps.com/index.php/home/article/view/4199">https://iirps.com/index.php/home/article/view/4199</a>



  
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## A Contemporary Overview of PPAR $\alpha/\gamma$ Dual Agonists for the Management of Diabetic Dyslipidemia



Pitchai Balakumar<sup>1,\*</sup>, Nanjaian Mahadevan<sup>2</sup> and Ramanathan Sambathkumar<sup>1</sup>

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**Abstract:** **Background:** Diabetes mellitus and concomitant dyslipidemia, being referred to as 'diabetic dyslipidemia', are the foremost detrimental factors documented to play a pivotal role in cardiovascular illness. Diabetic dyslipidemia is associated with insulin resistance, high plasma triglyceride levels, low HDL-cholesterol concentration and elevated small dense LDL-cholesterol particles. Maintaining an optimal glucose and lipid levels in patients afflicted with diabetic dyslipidemia could be a major task that might require a well-planned diet-management system and regular physical activity, or otherwise an intake of combined antidiabetic and antihyperlipidemic medications. Synchronized treatment which efficiently controls insulin resistance-associated diabetes mellitus and co-existing dyslipidemia could indeed be a fascinating therapeutic option in the management of diabetic dyslipidemia. Peroxisome proliferator-activated receptors  $\alpha/\gamma$  (PPAR $\alpha/\gamma$ ) dual agonists are such kind of drugs which possess therapeutic potentials to treat diabetic dyslipidemia. Nevertheless, PPAR $\alpha/\gamma$  dual agonists like miraglitazar, nateglitazar, tesaglitazar, ragaglitazar and aleglitazar have been reported to have undesirable adverse effects, and their developments have been halted at various stages. On the other hand, a recently introduced PPAR $\alpha/\gamma$  dual agonist, saroglitazar is an emerging therapeutic agent of glitazar class approved in India for the management of diabetic dyslipidemia, and its treatment has been reported to be generally safe and well tolerated.

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**Conclusion:** Some additional and new compounds, at initial and preclinical stages, have been recently reported to possess PPAR $\alpha/\gamma$  dual agonistic potentials with considerable therapeutic efficacy and reduced adverse profile. This review sheds light on the current status of various PPAR $\alpha/\gamma$  dual agonists for the management of diabetic dyslipidemia.

**Keywords:** PPAR $\alpha/\gamma$  dual agonists, insulin resistance, diabetic dyslipidemia, adverse effects, cardiovascular events, oedema.

### 1. INTRODUCTION

Dyslipidemia is a crucial menace for cardiovascular disease in patients afflicted with diabetes mellitus. The diabetic dyslipidemia is associated with high plasma triglycerides, reduced high-density lipoproteins (HDL), and elevated levels of small dense low-density lipoproteins (LDL) [1]. These changes could be caused by an increase in free fatty acid flux secondary to insulin resistance and be aggravated by elevation of inflammatory adipokines [1]. Principle consequence is required to prevent the incessant growing of morbidity and mortality associated with diabetes mellitus and hyperlipidemia across the world.

Peroxisome proliferator-activated receptors (PPARs) are documented as major regulators of lipid and glucose metabolism [2]. PPARs are the member of nuclear hormone

receptor superfamily that act as ligand-dependent transcription factors and expressively regulate the lipid and glucose metabolism. PPARs act on the DNA response elements as heterodimers with the nuclear retinoic acid receptor to modulate the expression of a target gene. Three isoforms of PPARs have been recognized namely PPAR $\alpha$ , PPAR $\gamma$  and PPAR $\delta$  [3, 4]. Activation of PPAR $\alpha$  decreases triglyceride levels, whereas activation of PPAR $\gamma$  causes insulin sensitization to enhance glucose metabolism (Fig. 1). Fibrate class of hypolipidemic drugs activates PPAR $\alpha$ , while thiazolidinedione class of antidiabetic agents activates PPAR $\gamma$  [5-7]. Patients with diabetes mellitus are at higher risk of having the cardiovascular disease onset. In addition, the cardiovascular disease risk is further high in those diabetic patients afflicted with hyperlipidemia [8]. Therefore, diabetic dyslipidemia is a major concern and needs an optimal therapeutic strategy for consistent management. Concurrent activation of PPAR $\alpha$  and PPAR $\gamma$  alongside targeting both lipid and glucose metabolism could be a beneficial therapeutic option for the management of diabetic dyslipidemia (Fig. 1). In view of this

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## REVIEW ON HYPOTHESIS, PATHOPHYSIOLOGY OF SCHIZOPHRENIA, AND ROLE OF INS IN ITS MANAGEMENT

AMURTHY N.

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schizophrenia, Vitamin B, Vit.

es about the literatures, including the role of vitamin supplementation in schizophrenia. Evidence is suggesting that supplementation includes Vitamin A, Vitamin D, Vitamin E, Vitamin B complex, and Vitamin C may be important in treatment. Patients may have increased levels of homocysteine (Hcy), due to the polymorphism in methylenetetrahydrofolate reductase (MTHFR) and N-methyl-D-aspartate receptors. The vitamins main effects are reduced the Hcy level and maintain dopamine and serotonin levels. In addition, B vitamins including B6, B9, and B12 and also Vitamin D can significantly reduce schizophrenia more than standard treatments alone.







## Invited Review

## A potential role of the renin-angiotensin-aldosterone system in epithelial-to-mesenchymal transition-induced renal abnormalities: Mechanisms and therapeutic implications\*

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## ARTICLE INFO

## ABSTRACT

**Keywords:**  
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Renal epithelial-to-mesenchymal transition  
Renal fibrosis  
RAAS interventions

Epithelial-to-mesenchymal transition (EMT) is an orchestrated event where epithelial cells progressively undergo biochemical changes and transition into mesenchymal-like cells by gradually losing their epithelial characteristics. EMT plays a crucial pathologic role in renal abnormalities, especially renal fibrosis. A number of bench studies suggest the potential involvement of renin-angiotensin-aldosterone system (RAAS) in renal EMT process and associated renal abnormalities. EMT appears to be an important pathologic mechanism for the deleterious renal effects of angiotensin II and aldosterone, the two major RAAS components. Mechanistically, the renal RAAS-TGF- $\beta$ -Smad3 signalling pathway plays an important pathologic role in EMT-associated renal abnormalities. Intriguingly, the RAAS antagonists such as losartan, telmisartan, eplerenone, and spironolactone have the potential to prevent renal EMT in bench studies. This review describes the key mechanistic role of RAAS overactivation in EMT-induced renal abnormalities. Moreover, drugs interrupting the RAAS at different levels in the cascade ameliorating the EMT-associated renal abnormalities are described.

## 1. Introduction

Epithelial-to-mesenchymal transition (EMT) has been suggested as an essential process for embryonic development, gastrulation and some organ development, and it is also implicated in tissue repair, cancer progression and organ fibrosis [1]. EMT is a programmed process whereby epithelial cells are known to acquire a mesenchymal cell (fibroblast-like) phenotype [1]. A growing body of evidence supports that EMT is involved in renal pathogenesis, particularly in renal fibrosis [2,3]. EMT also plays an imperative role in renal interstitial fibrosis in diabetic nephropathy [4]. Moreover, the EMT of tubular cells into a myofibroblastic phenotype is considered a key mediator of renal

scarring in chronic nephropathy [5]. Apart from diabetic nephropathy [6], EMT plays a key role in renal abnormalities including obstructive nephropathy [7], polycystic kidney disease [8] and hypertensive nephroangiosclerosis [9]. Traditionally, the chronic kidney disease burden has been largely associated with chronic hypertension and uncontrolled diabetes mellitus. On the other hand, non-traditional risk factors such as genetic or environmental factors may predominate in some regions and populations that could contribute to the epidemics of chronic kidney disease [10]. Environmental factors that are potentially associated with the development of chronic kidney disease include heavy metals such as lead, cadmium, arsenic, mercury and uranium, environmental and agricultural chemicals, industrial wastes,

**Abbreviations:** ACE, angiotensin-converting enzyme;  $\alpha$ -SMA, alpha-smooth muscle actin; Ang (1-7), angiotensin (1-7); Ang II, angiotensin II; AT<sub>1</sub> receptor, angiotensin II-type 1 receptor; ECM, extracellular matrix; EGFR, epidermal growth factor receptor; EMT, epithelial-to-mesenchymal transition; ERK, extracellular signal-regulated kinase; FSP-1, fibroblast-specific protein-1; MAF, 25-O-methylalisol F; miRs, microRNAs; NRK52E, normal rat tubular epithelial cell lines; PPAR $\gamma$ , peroxisome proliferator-activated receptor gamma; PZA, porcine acid ZA; RAAS, renin-angiotensin-aldosterone system; SHR, spontaneously hypertensive rats; TGF- $\beta$ , transforming growth factor-beta

\* This article reflects the views of the author (G.J) and should not be construed to represent FDA's views or policies.

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**REVIEW ARTICLE**

**A Review on Relevance of Herbal Medications for Psychiatric Patients**

**Aswathi T<sup>1</sup>, Venkateswaramurthy. N<sup>2\*</sup>, Sambath Kumar. R<sup>3</sup>**

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**ABSTRACT:**

**Objective:** This review illustrates on the use of herbal medication and its impact among psychiatric patients.

**Method:** PubMed was searched for articles related to the herbal remedies used in the psychiatric patients. A secondary search was performed using references obtained from articles published from 2000 – 2017 identified by the PubMed search. Articles focusing on the experimental trials in adults and those patients who were not on medication was excluded during the selection process and those articles which aimed in assessing the incidence of drug interaction and possible negative effects due to co-administration of herbal medications with psychiatry drugs was included in this review. **Result and Discussion:** Effective studies have shown that additional alternative treatment with particularized herbal medicine increases antidepressant response and that reduces certain side effects associated with psychotropic medications. Herbal medicines used for the treatment of psychiatric problems was produced safe and effective towards severe depressive episodes, but usage of these herbal drugs in patients with mental illness led to unusual occurrence of side effects. This review also discusses the pharmacological mechanism of drug interaction of various herbal medications. **Conclusion:** This review gives an insight of the importance in increasing the knowledge of the health care professionals of the safety and efficacy of psychiatric drug use with herbal medication, at the same time it is also important to provide information to the patients regarding the benefits and contraindications of these herbal remedies when accessed with the other psychiatric medications.

**KEYWORDS:** Herbal remedies, Psychiatry, Gamma-aminobutyric acid (GABA), Dopamine (DA), Noradrenalin (NA), Serotonin (5-HT), Central Nervous System (CNS).

**INTRODUCTION:**

Psychiatric disorders are one of the most common typical prevalent diseases in our society, and according to World Health Organization it may become a primary cause of affliction in the future even though there is a wide range of psychiatric medications being used, which was not effective with all patients pharmacologically and psychotherapeutically<sup>1</sup>.

In many countries of the world, natural medicine remains the most available and sometimes the only form of medical care when mental health is concerned. Herbs are concurrently used with prescribed medications by patients worldwide. Studies have shown that many natural herbs was effective as standard psychiatric drugs in clinical trials that was performed in laboratories, even though most clinicians are unaware of their pharmacological mechanisms<sup>2</sup>.

In order to treat and counter mental illness, there were many natural herbs containing vitamins, minerals and antioxidants. Many studies revealed that a range of plant medicines indicated to produce probable efficacy<sup>3</sup>. Herbal medication remedies may be encountered in order to treat psychiatric problems; that produce

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**REVIEW ARTICLE**

## **A Review on the Effect of Immunosuppressants on Fertility**

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### **ABSTRACT:**

**Background:** Infertility is defined as not being able to get pregnant (conceive) after one year (or longer) of unprotected sex. Many studies had showed that extensive use of immunosuppressant's may result in infertility. Immunosuppressive drugs are used in the treatment of inflammatory and autoimmune diseases, as well as in transplantation. Frequently prescribed in young people, these treatments may have deleterious effects on fertility, pregnancy outcomes and the unborn child. **Aim:** The aim of this study is to review the literatures depicting the about immunosuppressant's, its impact on fertility and related pregnancy outcomes. **Methods:** A systematic literature search of the Pub Med database was performed using a combination of relevant terms related to 'infertility', 'conception', 'reproduction', 'immunosuppressant's. **Conclusion:** From the review of many literatures this study concludes that immunosuppressants has varying effect on pregnancy. Some of the immunosuppressants at therapeutic doses can cause infertility when used for a long time.

**KEYWORDS:** Fertility, reproduction, conception, immunosuppressants.

### **INTRODUCTION:**

Infertility is a term used to define as a disease of the human reproductive system where the body fails to achieve pregnancy after sexual intercourse. World health organization (WHO) has reported infertility as a chronic health disorder which affects both men and women all across the world.<sup>1</sup>

Infertility is a condition which do not induce any pain, morbidity, or physical restrictions. But many studies had revealed that infertility can cause emotional and behavioural changes. The psychological and social impact of the problems caused by the infertility not only affect the patients but also their partners are equally affected and this is a cause for many distress for health professionals.

The incidence of infertility has been increased over the past decades and many healthcare professionals admit that the incidence of infertility will increase in the coming years. Due to the increased prevalence and distressing impact infertility has been included as a spot lit programme in events for reproductive and children's health in India.<sup>2,3</sup>

Various factors affect fertility such as the age of couple, frequency of coitus, sexual exposure. Among the normal couples married at the age of 23-25, 25% of them have a chance to get pregnant after indulging in unprotected sexual intercourse and vast majority of the couples get pregnant within the 1<sup>st</sup> year. In a country like India only less than 5% of the people delay their conception to two years and more.

Both genders are equally responsible for the causes of infertility. About 45 percent of couples face infertility problems as it not only limited to women, the most common problems men face are low sperm count, morphology abnormalities and low motility of sperm. Several factors contribute to infertility including

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**REVIEW ARTICLE**

## **A Review on the Irrational Antibiotics usage in Pediatrics for Respiratory Tract Infections**

**Wilma Mary Thomson<sup>1</sup>, M. Sudha<sup>2\*</sup>, N. Venkateswaramurthy<sup>3</sup>, R. Sambath Kumar<sup>4</sup>**

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### **ABSTRACT:**

This review highlights the increased prevalence of antibiotic use for respiratory tract infections, since nowadays respiratory tract infections (RTIs) especially in children have been found to be one of the most frequent reasons for parents to consult the healthcare professionals. The etiological cause of such infections in children has been seen to be viral but unnecessary use of antibiotics in such cases has led to irrational prescribing pattern of antibiotics and such inappropriate use of antibiotic in both quantity and drug choice has greatly influenced the development of antibiotic resistance in children. Thereby, treating respiratory tract infection in children with proper medication guidelines has been mandatory for the physicians.

**KEYWORDS:** Respiratory Tract Infection; Antibiotics; Guidelines; Irrational prescription; Antibiotic Resistance.

### **INTRODUCTION:**

Any infectious disease on the respiratory tract is termed as Respiratory Tract Infections. RTIs remain as a challenge to the public health in both industrialized and developing countries because of their frequency and economic impact [1].

Infections of the respiratory tract are grouped according to their symptomatology and anatomic involvement (Figure 1) It is usually classified as URTIs (Infection site includes nasal cavity, pharynx and larynx) and LRTIs (Infection site includes trachea, primary bronchi and lungs).

Infections of the respiratory tract are grouped according to their symptomatology and anatomic involvement (Figure 1) It is usually classified as URTIs (Infection site includes nasal cavity, pharynx and larynx) and LRTIs (Infection site includes trachea, primary bronchi and lungs).

Depending on the Global Burden of Disease 2015 study (GBD 2015), the upper respiratory tract infections (URTIs) such as chronic obstructive pulmonary disease (COPD) and lower respiratory tract infections (LRTIs) such as acute bronchitis, pneumonia and bronchiectasis ranks the third and fourth place for the causes of death, after cardiac diseases and cerebrovascular diseases respectively [2]. The aetiological cause of RTI being viral, it is noted that some doctors prescribe newer and broad-spectrum antibiotics early before diagnosis because they believe that, these antibiotics would give patients the best option of fast cure and it could help the patient to prevent hospital admissions.

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## AN OBSERVATIONAL STUDY OF MEDICATION ERRORS AMONG PSYCHIATRIC PATIENTS IN A TERTIARY CARE HOSPITAL

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### ABSTRACT

**Objective:** The objective of this study is to evaluate the common medication error (ME), and its causes, category, and severity by using suitable questionnaire.

**Methods:** A prospective observational study was carried out for 6 months in a psychiatric department. Demographic data, clinical history, and complete prescription were noted.

**Results:** A total of 120 psychiatric cases were collected, among that 116 MEs were identified in which male patients were 64 (55%) and females 52 (44.8%). The number of MEs occurred due to physician was 67 (57.7%), due to nurses was 15 (12.9%), and combined was 38 (32.7%). Incomplete prescription was the main type of error that we found. About 43.1% of the error we identified was informed to the staff and no specific action was needed for 37.1% of errors. In our study, we found that majority of 54 (46.5%) errors were categorized under category B, but there was no harm to the patient.

**Conclusion:** The present study concluded that most of the patients admitted in the psychiatry department would experience MEs. Clinical pharmacist can play a major role in the early detection and prevention of MEs and thus can improve the quality of care to the patients.

**Keywords:** Medication errors, Morbidity, Mortality, Psychiatry.

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### INTRODUCTION

Safety is a global idea that encompasses performance, protection of care, reactivity of caregivers, and pleasure of sufferers and family. Patient protection has emerged as a major goal for health-care development. The idea of quality has advanced from a method grounded within the physician-patient relationship to broader techniques related to the health-care community, concept of efficiency, and moral access to care [1]. Medication error (ME) is defined as "any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the healthcare professional, patient. Such events may be related to the professional practice, health-care products, procedures, and systems including prescribing, order communication, product labeling, packaging, compounding, dispensing, distribution, administration, education, monitoring, and use" [2]. ME in psychiatric patients, especially in long-term care facilities, is often trained in self-administration of medications to increase their self-care and to improve their compliance. However, psychiatry patients are extraordinarily at risk of medication mistakes as they are prescribed with complex medication regimen, may be non-compliant, and resist medicinal administration or even be violent. Medication administration to psychiatric inpatients is a demanding situation when compared with other inpatients. Evidences from a plethora of resources throw light onto a range of adverse drug events (ADEs) which are due to MEs from psychiatric drugs [3]. MEs might also occur at any level of prescribing, documenting, or management. Furthermore, MEs also contribute to morbidity, mortality, and exceeded fitness care prices. Mistakes can happen in all stages of care technique from diagnosis to drug management. Blunders arise as a result of two types of failure; the right action does not proceed as meant (an error of execution) or the unique meant action is not accurate (errors of planning). ADEs and MEs are spotted as a crucial and extensive trouble in modern health

center settings, inflicting damage as well as avoidable morbidity and mortality [4].

MEs represent the largest single cause of errors in the hospitals, which can be result from the interaction of multiple factors including nature of works environment, difficulty of tasks involved, lack of knowledge on MEs, lack of experience, and lack of required equipment. It is clinically evident that both individual factors contribute almost the same to the ME occurrence [5].

The most common errors have been unauthorized tablet crushing, omission without a valid cause, and failure to file administration. Direct observation is useful, and sensitive technique for detecting medication administration errors in psychiatry is found useful [6]. MEs are one of the most common types of patient incidents worldwide that may cause harm to the patients. To our knowledge, few studies have been completed in psychiatric health center placing which Status on MEs in more ranges of the scientific device. A specific estimation of kinds and capability severity of errors are wanted to select relevant interventions to lessen the MEs. The existing studies were undertaken to understand different kinds of ME in psychiatric prescriptions. This present study aimed to evaluate and categorize the ME occurred in the psychiatric department of a tertiary care hospital.

### METHODS

The prospective observational study was carried out for a period of 6 months in a tertiary care hospital, Erode, Tamil Nadu. The ethical clearance for the study was obtained from the Institutional Ethical Committee. Based on inclusion (patients admitted to the psychiatric department during the study period) and exclusion criteria (patients with other comorbid conditions, pregnant, and lactating women were



  
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**ASSESSMENT ON PREVALENCE OF HYPERTENSION AND ITS ASSOCIATED RISK FACTORS ALONG WITH MMAS SCORE IN A RURAL COMMUNITY: A HOME BASED SCREENING**

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**ABSTRACT**

**Objectives:** In India, a study on hypertension (HTN) prevalence conducted in a community over a period of 3-6 decades showed an increase of 30% in urban population and 10% in rural population. The study aimed to assess the prevalence of HTN and pre-HTN in a rural community and also to find the significance of risk factors which precipitate to it.

**Methods:** This cross-sectional study was conducted in a rural community of Salem district, Tamil Nadu, India. HTN and pre-HTN was defined by the Joint National Committee 8<sup>th</sup> report guidelines. Patient data's (sociodemographic variables, lifestyle factors, and medical reports) were collected with the help of questionnaire. Identified hypertensive patients were assessed with MMAS-8 questionnaire.

**Results:** During the study period of 8 months, 425 subjects were screened and studied for HTN and pre-HTN. More than half (59.4%) of the study group were found to be hypertensive. Of the 295 reported cases, 228 (53.6% of 425) were "known" cases of HTN and 67 (15.8% of 425) were newly diagnosed cases. A positive association ( $p < 0.05$ ) was observed between HTN and age, body mass index (BMI), alcohol, and tobacco use other than smoking. 75 patients were found to be prehypertensive, in that 57.3% (43 cases) were male and 42.7% (32 cases) were female. Majority of hypertension patients (66%) were with low adherence than 24% medium and 10% high adherence towards their medications.

**Conclusion:** Our study concluded that the prevalence of pre-HTN and HTN was higher among the study population, so there is a need for screening of individuals at the early age group. Further studies are needed to observe and confiscate the reasons why majority of hypertensive patients with low medication adherence.

**Keywords:** Prevalence, Prehypertension, Hypertension, Body mass index.

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**INTRODUCTION**

Hypertension (HTN) is one of the predominant global risks for mortality and is seen with a drastic rise in developing nations in accordance with rise in age [1]. In 2005, a worldwide data showed that 639 million patients with HTN are seen in low- and middle-income countries and estimated to victimize more than 1.56 billion by 2025 [2]. In India, HTN prevalence conducted in community over a period of 3-6 decades showed an increase of 30% in urban population and 10% in rural population [3]. This increase is attributed to the rapid epidemiological transition accompanied by urbanization, which is occurring in India [4]. Overweight and obesity showed impact on HTN on various studies [5].

HTN, being a major risk factor for cardiovascular diseases, is an important issue of medical and public health. It is the most common condition seen in primary care which leads to myocardial infarction, stroke, renal failure, and death if not detected early and treated appropriately [6]. HTN is the most common comorbidity of diabetes and vice versa [7]. HTN exerts a substantial public health burden on cardiovascular health status and health-care systems in India [8]. Annually, it causes 7.1 million (one third) of global preventable premature deaths [9].

Unfortunately, there is still inadequate awareness about the real dimension of the problem among the general public. Most of the people in the rural community are illiterates, so they will not be aware of various disease states, their progression, and complications. Hence,

an attempt was being made to find the prevalence and associated risk factors of HTN and pre-HTN in rural population.

**METHODS**
**Research period**

This study was a community-based cross-sectional study, carried out in Valayakaranur and Vattamalai, rural villages near Kumarapalayam town, Salem district, Tamil Nadu, India, for a period of 8 months from September 2016 to April 2017.

**Inclusion and exclusion criteria**

The study population was selected according to the inclusion criteria. Inclusion criteria included non-pregnant population between 35 and 75 years of age. Subjects for hypertensive screening were selected according to the questionnaire, willing to undergo screening tests, providing a signed consent, and population already diagnosed diabetes and undiagnosed HTN. Patients on antihypertensive medication and who refused to participate were excluded from the study. All the studies were conducted in accordance with the guidelines for Good Epidemiological Practices and after getting approval from the institutional ethical committee.

**Appraisement**

Based on inclusion criteria, the house-to-house survey was conducted in rural villages. In questionnaire-based survey, details such as patient name, age, gender, present complaints, family history, blood pressure (BP), social history, exercise pattern, and other risk factors associated with HTN were enrolled by interviewing the participants. Medication



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## Pharmacological Research

Volume 144, June 2019, Pages 132-141

Review

## Molecular targets of fenofibrate in the cardiovascular-renal axis: A unifying perspective of its pleiotropic benefits

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Abdulrhman Alsayari<sup>b</sup> , Nallasamy Venkateswaramurthy<sup>a</sup> , Sokkalingam A. Dhanaraj<sup>c</sup>

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### Abstract

The activation of peroxisome proliferator-activated receptor  $\alpha$  (PPAR $\alpha$ ) is a key pharmacological drug target for dyslipidemic management. Dyslipidemia is associated with abnormal serum lipid profiles viz. elevated total cholesterol, high triglyceride, elevated low-density lipoprotein cholesterol, and reduced high-density lipoprotein cholesterol levels. Fenofibrate, a third-generation fibrat acid derivative, is an activator of PPAR $\alpha$  indicated for the treatment of mixed dyslipidemia and hypertriglyceridemia in adults. Fenofibrate is considered an important lipid-lowering medication employed in patients afflicted with atherogenic dyslipidemia. Intriguingly, recent bench studies have demonstrated an array of cardiovascular and renal pleiotropic beneficial activities of fenofibrate, besides its foremost lipid-lowering action. The activation of PPAR $\alpha$  by fenofibrate could negatively regulate the cardiomyocyte hypertrophy. In addition, fenofibrate has been suggested to have a protective effect against experimental ischemia/reperfusion injury in the myocardium in part via endoplasmic reticulum stress inhibition. Fenofibrate has also been shown to suppress arrhythmias in isolated rat hearts subjected to ischemic/reperfusion-induced cardiac injury. Moreover, in a rat model of metabolic syndrome and myocardial ischemia, fenofibrate therapy has been shown to restore antioxidant protection and improve myocardial insulin resistance. Furthermore, studies have highlighted the pleiotropic vascular endothelial protective and antihypertensive actions of fenofibrate. Interestingly, recent bench studies have demonstrated renoprotective actions of fenofibrate by implicating diverse mechanisms. This review sheds light on the current perspectives and molecular mechanistic aspects pertaining to the cardiovascular pleiotropic actions of fenofibrate. Additionally, the renal pleiotropic actions of fenofibrate by focusing its possible modulatory role on renal fibrosis, inflammation and renal epithelial-to-mesenchymal transition have been enlightened.

### Graphical abstract

<https://www.sciencedirect.com/science/article/abs/pii/S1043661819302762>

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REVIEW ARTICLE

## Pharmacogenetics and Genetic Polymorphism of CYP Enzymes in Indian Population: A Clinical Review

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**ABSTRACT:**

Pharmacogenetic polymorphism results from the mutations in a Cytochrome P450 (CYP) gene leading to functional alterations, such as increased or decreased activity and occurs at a frequency of at least one percent in a population. At present clinical situation drug clearance and inter-individual variation in drug response is a usual and complex problem. In this clinical review there is a fast update on pharmacogenetics and genetic polymorphism of CYP enzymes in Indian population.

**KEYWORDS:** CYP 450, Pharmacogenetics, Allele, polymorphism.

**INTRODUCTION:**

Pharmacogenetic polymorphism is acquiring a trait with a single genetic locus with two alleles, where the slightest common allele has an incidence of about 1% or greater. Genetic polymorphism in a population is a result of more than one allele occupies a gene's locus and can be discovered at the genotype level and/or the phenotype level based on change denzyme function.<sup>[1]</sup> CYP superfamily encompasses drug metabolizing enzymes that can be involved in complex process such as hydrolysis, oxidation and reduction in which the functional groups of a substrate are added or deleted in phase I.

The CYP450 family encompasses 18 families and 44 subfamilies consisting up of 57 genes and 58 pseudo genes. Among them, 90 percent of drugs undergo the oxidative reactions by CYP1 which encompasses CYP subfamilies.

CYP 450 enzymes are participated in the oxidative uptake of endogenous complexes such as fatty acids, leukotrienes (LTs), steroids, prostaglandins (PGs) and in the digestion of foreign elements such as carcinogens, drugs, and environmental pollutants.<sup>[1]</sup> Genetic polymorphisms seen in drug-metabolizing enzymes are the main basis of variability that leads to the event of adverse events and decreased therapeutic efficacy.<sup>[1]</sup> About 50 human CYP isozymes have been recognized to date.<sup>[4]</sup> About 20 of these genes are functionally polymorphic comprising CYP2D6, CYP2A6, CYP2C19 and CYP2C9.

Subsequently, about 40 percent of CYP-dependent drug metabolism is performed by polymorphic enzymes. Overlapping substrate specificity of enzymes, an assembly of single nucleotide polymorphisms (SNPs) and distinctions among ethnic groups make likelihood of phenotypic drug response difficult.<sup>[5,6]</sup> By adjusting drug dosage and dose of each individuals, treatment failure and unnecessary toxicity can be avoided.<sup>[7]</sup> India, the world's succeeding greatest densely inhabited country with 1.21 billion humans, including 4,693 communities, 325 languages and 25 scripts and have extreme diversity in terms of languages, social characteristics, culture, biological, and religions in Indians and genetically they are unique from other races. Based on their national origin, Indian populations are morphologically classified

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## Pharmacologically relevant drug interactions of sulfonylurea antidiabetics with common herbs

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### ABSTRACT

**Introduction:** Sulfonylurea antidiabetics are insulin secretagogues useful in the treatment of type 2 diabetic patients. The probability of adverse drug interactions is high in patients taking sulfonylureas and other drugs including herbal medicines. The present review is aimed to present the herbal drugs having interacting potentials with sulfonylurea antidiabetics.

**Methods:** The databases such as PubMed, Google Scholar, Science Direct, Directory of open access journals (DOAJ) and reference lists were searched using the keywords drug interactions, Sulfonylureas, pharmacodynamic interactions, antidiabetic herbs, pharmacokinetic interactions and CYP2C9.

**Results:** Sulfonylureas are primarily metabolized by CYP2C9 enzyme and the herbs like St. John's wort and *Ginkgo biloba* induce CYP2C9-mediated metabolism of sulfonylureas while fruit juices like Pomegranate juice and Pineapple juice inhibit their metabolism. In addition, the antidiabetic herbal supplements such as Bitter melon, Fenugreek, Cinnamon, Gymnema, Ginseng, Ginger, Garlic, *Aloe vera*, Sesame, *Andrographis paniculata* and Neem potentiate the hypoglycemic activity of sulfonylureas, pharmacodynamically.

**Conclusion:** Some herbal supplements are capable of interacting pharmacokinetically and pharmacodynamically with sulfonylurea antidiabetics.

#### Implication for health policy/practice/research/medical education:

Due to the possible interaction of herbal supplements with sulfonylurea antidiabetics, prescribers and pharmacists are required to be aware of these drug interactions to avoid the possible problems for patients.

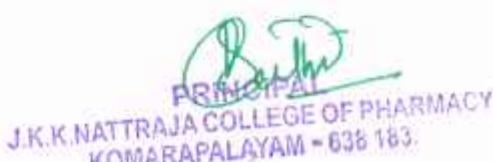
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### Introduction

Diabetes mellitus (DM) is a chronic metabolic condition in which hyperglycemia is noted for a longer duration (1). It is a global health burden and the incidence of diabetes among global population is increasing every year. It has been estimated that 171 million of world population were affected by diabetes in the year of 2000 (2), 285 million in 2010 (3), 366 million in 2011 (4), 382 million in 2013 (5), 415 million in 2015 (6) and 451 million in 2017 (7). The prevalence of diabetes around the globe has been projected as 552 million by 2030 (8), 592 million by 2035 (9), 642 million by 2040 (10) and 693 million by 2045 (11). DM is sorted mainly as type 1 DM which is insulin-dependent (IDDM) and type 2 DM, the non-insulin

dependent (NIDDM). DM could be managed by both non-pharmacological and pharmacological therapies. Non-pharmacological management of diabetes includes lifestyle modifications such as dietary interventions, increased physical activity and smoking cessation. (12). Type 1 diabetes is managed pharmacologically by administering insulin injections mainly and the pharmacological management of type 2 diabetes includes the use of antidiabetic medications such as metformin, sulfonylureas, meglitinides (repaglinide and nateglinide), thiazolidinediones (rosiglitazone and pioglitazone), alpha glucosidase inhibitors (acarbose and miglitol), dipeptidyl peptidase 4 (DPP4) inhibitors (sitagliptin, saxagliptin, linagliptin, etc), SGLT2 inhibitors (dapagliflozin,

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## REVIEW ON CLINICALLY DEVELOPING ANTIBIOTICS

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## ABSTRACT

The world is running out of antibiotics. Between 1940 and 1962, more than 20 new classes of antibiotics were marketed. Since then, only two new classes of antibiotics were marketed. Now, not enough analogues are reaching the market to stem the tide of antibiotic resistance, particularly among gram-negative bacteria which indicates the need of novel antibiotics for their effective action. This review describes those antibiotics in late-stage clinical development. Most of them belong to existing antibiotic classes and a few with a narrow spectrum of activity are novel compounds directed against novel targets. The reasons for some of the past failures to find new molecules and a path forward to help attract investments to fund the discovery of new antibiotics are described.

**Keywords:** Antibiotics, Clinical development, Narrow spectrum

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## INTRODUCTION

The antibiotics are the cornerstones of recent medicine after the entry of penicillin, which came into widespread use in the beginning of the 1940s. [1] By 1950s, multiple numbers of newer classes of antibiotics came into the scene, over the next twenty years. [2] Nowadays it is difficult to treat and do certain medical procedures

which are extensively used, like chemotherapy, organ transplants, joint operations or the provision of care for premature babies without the antibiotics [1]. Moreover, they can control both morbidity and mortality rate in humans and animals. [3] To brief outing, they have become the lifesaving treatment for all types of infections in humans as well as animals. The timeline of new class antibiotics has been given in table 1.

Table 1: Time line of antibiotics

Year introduced	Class of drug
1935	Sulphonamides
1941	Penicillins
1944	Aminoglycosides
1945	Cephalosporins
1949	Chloramphenicol
1950	Tetracyclines
1952	Macrolides/lincosamides/streptogramins
1956	Glycopeptides
1957	Rifamycins
1959	Nitroimidazoles
1962	Quinolones
1968	Trimethoprim
2000	Oxazolidinones
2003	Lipopeptides

Now, however, two developments are resulting in more and more difficult to treat the bacterial infections with the antibiotics successfully, including the increasing number of antibiotic-resistant pathogens and the second one is that the number of new antibiotics developed since the 1970s has decreased [4]. It was estimated that infections that can be treated completely are also becoming more complicated to treat, increasing costs of healthcare facilities, and patient mortality is increasing with costs to the society. The antibiotic effectiveness has to decrease now and many of the microorganisms are resistant to multiple antibiotics [5]. The issue of antibiotic resistance, though not new, has amplified in the previous 10 to 15 y and creates a serious threat to the treatment of infections. Certain new investigational studies were reported that, among all the multidrug-resistant pathogens like *S. aureus* and *P. aeruginosa*, *Acinetobacter* species are the major infective organism which can cause even life-threatening resistant infections. The improper intake of antibiotic dosage or lack of sensitive antibiotic agents to fight against these types of organisms may be the reason for the occurrence of such infections [6].

Despite this increase in the multidrug-resistant pathogens, the development of antibacterial agents is declining, [7] that is, there are not enough antibiotics for treating such infections [4]. This antibiotic deficit will become more and more problematic in the years to come.

As per World Health Organization (WHO), the antibiotic resistance is one among the serious hazard to human health and the consequences of antibiotic-resistant bacterial infections are greater than ever [4]. So, new antibiotics are critically needed to alleviate the problems associated with this antibiotic resistance [8, 9]. The Infectious Diseases Society of America (IDSA, 2010) estimated that at least another 10 antibiotics, which are active against these superbugs, are required to enter the market within ensuing ten years [10]. It ought to be noted that antibiotics, which were already in market use are complex natural products with multiple binding sites on the target, making it less likely for resistance selection. Moreover, the prevalence of treatment difficulty for both resistant and multi-resistant nosocomial organisms are greatly rising, both for Gram-negative and Gram-positive bacteria among this; gram-negative organisms are producing a greater threat [11].





## Role of chloroquine as an anticancer agent

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### ABSTRACT

Chloroquine is a prototype antimalarial drug used to prevent and treat malaria, amebiasis and other autoimmune disorders such as rheumatoid arthritis and systemic lupus erythematosus. The drug acts as an autophagy inhibitor where autophagy is a self-destructive process which is needed to balance sources of energy at developmental process and in response to nutrient deprivation. New studies have shown the crucial role of chloroquine in cancer treatment and is been extensively used as a monotherapy or adjunct therapy in various types of cancer. This review summarizes the role of chloroquine and its action as an autophagy inhibitor in cancer treatment and also the various safety issues concerning with the same.



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iting lysosomal protease leads to autophagy blockade and further preventing autophagosome-lysosome fusion events have made a greater acceptance as an autophagy inhibitor in vitro and in vivo (Amaravadi et al., 2011).

### Autophagy

Autophagy is defined as a group of mechanism involved in the regulation of cell and tissue homeostasis. It has a major role in many physiological functions such as development, differentiation, normal growth and immunity.

It is an intercellular degradation system which is required to balance energy during phases of development and also in response to nutrient stress. It also degrades damaged or unwanted proteins and cellular organelles. Cancer cells are thought to use autophagy as a source of energy in the unfavorable metastatic environment. This mechanism enables cancer cells to use autophagy as a source of energy in unfavourable conditions.

Chloroquine helps tumor cells to overcome stressors in the tumor microenvironment and also the injuries caused due to endocrine therapy, chemotherapy and radiation therapy. Therefore, it functions as a cell-survival pathway. It also supports the progression and metastatic dissemination of established tumors (Manic et al., 2014). Since the cancellation of autophagy via knockdown of

### INTRODUCTION

Chloroquine is a quinolone derivative which is used to treat malaria. It exerts its action by inhibiting the heme polymerase activity which in turn leads to the increase of free heme. This has lethal effects for the parasite and disrupts its membrane function. It may also interfere with the biogenesis of nucleic acids within the parasite. It is extensively used in the treatment of all types of malaria except for those caused by chloroquine resistant *Plasmodium falciparum*. This drug also has potential anti-cancer properties when given as a monotherapy or as an adjuvant therapy with other anticancer agents for the treatment of various types of cancer. Chloroquine is an autophagy inhibitor and hence used as a novel anticancer drug. Its action in inhib-



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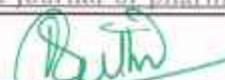
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4	COMPARISON OF ANTIHYPERTENSIVE COMBINATION THERAPY AND GLYCEMIC CONTROL IN DIABETIC HYPERTENSIVE PATIENTS	Mrs. P. Sujitha	JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH	2019	0975-1459	<a href="https://www.jpsr.pharmainfo.in/Document/Downloads/Volumes/vol11issue07/jpsr11071929.pdf">https://www.jpsr.pharmainfo.in/Document/Downloads/Volumes/vol11issue07/jpsr11071929.pdf</a>	<a href="https://www.jpsr.pharmainfo.in/Document/Downloads/Volumes/vol11issue07/jpsr11071929.pdf">https://www.jpsr.pharmainfo.in/Document/Downloads/Volumes/vol11issue07/jpsr11071929.pdf</a>



  
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## ASSESSMENT AND EDUCATIONAL INTERVENTIONS IN INHALATION TECHNIQUE AMONG ASTHMA AND COPD PATIENTS AT A TERTIARY CARE HOSPITAL IN ERODE (Tamilnadu- India)

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### ABSTRACT

The aim of this research was to assess the quality of inhalation technique in patients and to determine the effect of a single intervention by clinical pharmacist to improve knowledge of patient regarding the use of inhalers among asthma and Chronic Obstructive Pulmonary Disease (COPD) patients. A total of 223 patients with asthma or COPD using inhaler medication were randomly selected. During the first appointment, patients were interviewed and their inhalation technique was assessed with checklists. Errors were recorded and counselling with practical demonstration of proper inhalation technique was given. After 3 days, inhalation technique by the patients was reassessed and recorded using checklist. Pre and post comparison were performed to assess the impact of education by pharmacist about inhalation technique among asthma and COPD patients. All the patients committed at least single one error in their inhalation technique. There was a significant reduction in the number of patients who committed error in the first appointment to second appointment. Out of 223 patients, 162 patients (72.6%) committed error in the step 5 (exhale normally) in the first appointment. This number dropped to 21 (9.4%) in the second appointment after counselling with practical demonstration ( $P < 0.015$ ). Correct inhalation technique is essential for effective drug delivery in COPD and asthma. The inhalation technique of asthma and COPD in patients is poor. Pharmacists can play a pivotal role in improving health outcomes for patients with asthma and COPD by providing knowledge on how to use their inhaler devices properly.

**KEYWORDS:** Inhalers, inhalation technique, Intervention, Patient Education, Aerosol Therapy



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## ASSESSMENT OF QUALITY OF LIFE IN DIALYSIS AND NON-DIALYSIS CHRONIC KIDNEY DISEASE PATIENTS

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### Keywords:

Quality of life,  
Chronic renal failure, Dialysis

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**ABSTRACT:** Quality of life is an essential measure that proves the effectiveness of health care, health level, and well-being. Kidney diseases are one of the major health problems that affect Quality of life. This study aimed to assess the quality of life in dialysis (CRF-D) and non-dialysis (CRF-ND) chronic renal failure (CRF) patients using Kidney Disease Quality of Life-short form (KDQOL-SF<sup>TM</sup>) and identify the differences in disease symptoms between these two groups. 200 CRF patients were included in the study. Our findings showed that some symptom burden was higher in the non-dialysis group compared to the dialysis group, but most of the symptoms did not reach statistical significance. Similarly, our results indicate no differences in quality of life and symptoms between CRF patients with dialysis and without dialysis.

**INTRODUCTION:** Chronic renal failure is one of the slow, gradual, and irrevocable loss of renal function, contributing to the failure of kidneys to accomplish their basic functions. The incidence and prevalence in patients with chronic kidney disease (CKD) are growing worldwide. The problem is associated with high morbidity and mortality throughout the progression from the early stage of the disease. Although very much progress has been made in prevention, detection, and treatment, CKD remains a major public health issue. Its global prevalence is generally estimated at 5-10%. CKD prevalence is contentious. Statistics from the American National Health and Nutrition Examination Survey show that in the period of

1999 to 2004, the prevalence of CKD stages 1 to 4 increased significantly when compared to their previous report (13.1 versus 10.0%). Prevalence is increased mainly due to the aging population; it is also connected with increases in prevalence of hypertension and diabetes mellitus <sup>1-3</sup>. Because of cardiovascular morbidity and mortality, the global burden of CKD-associated diseases is alarmingly large.

The World Health Organization (WHO) has defined Quality of life (QOL) as "an individual's perception of their position in life in the context of the culture and value systems in which they live and about their goals, expectations, standards, and concerns" <sup>4</sup>. QOL is an important outcome, utilized as a valuable parameter to measure health and well-being. Research conclusions have shown that lower results on QOL were firmly associated with a higher risk of fatality and hospitalization than clinical parameters such as serum protein levels in cases of CKD sufferers. Numerous studies have shown that individual with CKD had reduced QOL

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# Comparison of Antihypertensive Combination Therapy and Glycemic Control in Diabetic Hypertensive Patients

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## Abstract

**Objective:** To compare the glycemic level in diabetic hypertensive patients who were on antihypertensive combination therapy and to evaluate utilization patterns of antihypertensive combination therapy among diabetic hypertensive patients in a government tertiary care hospital at Erode.

**Methods:** The prospective observational study was undertaken at the inpatient department in a tertiary health care hospital, Erode, Tamil Nadu. The study was performed for a six months period after obtaining clearance from J.K.K.Natraja College of Pharmacy's Ethical committee. A data entry form was prepared to record patient details like name, age, sex, educational status, life events, and social history and prescribed drugs. After obtaining informed consent form from the patient, the demographic data were collected. A total of 200 cases were collected and among that 112 patients were on antihypertensive combination therapy which included diuretics, beta blockers (BB), angiotensin converting enzyme inhibitors (ACEI's), and calcium channel blockers (CCB's). The glycemic level of 112 diabetic hypertensive patients under antihypertensive combination therapy was compared by taking their FBS and RBS reading.

**Result:** In this study out of 200 cases collected, 56 (28%) patients were on antihypertensive mono therapy and 112 (56%) patients were on antihypertensive combination therapy and the rest of the patients didn't know the medicines that they were taking. Here, out of 112 patients 35 patients had an elevated random blood sugar (RBS) reading (above 300 mg/dl). In these 35 patients, 20 patients (58.82%) were on diuretics (furosemide) and BB (atenolol) combination therapy. Fasting blood sugar level FBS level was elevated (above 200 mg/dl) in 45 patients. Wherein 26 patients (57.78%) were on diuretics (furosemide) and BB (atenolol) combination therapy. Finally, it was observed that the patients who were on diuretic (furosemide) therapy in combination with BB (atenolol) had an elevated blood glucose level in comparison with the patients who were on other antihypertensive combination therapy.

**Conclusion:** The most commonly used antihypertensive 2 drug combination therapy was CCB and BB (31.25%) followed by diuretics and BB (29.46%). This study shows CCB in combination with BB as the most commonly prescribed drug therapy for treating hypertension in patients with diabetes, after tabulating the data it shows that the patients under diabetic (furosemide) therapy in combination with beta blocker (atenolol) had an elevated blood glucose level in comparison with the patients under other antihypertensive combination therapy. Further, it was also observed that the most number of patients with comparatively lesser elevation in blood sugar level was under CCB and BB (atenolol).

**Keywords:** Diabetes Mellitus, Antihypertensives, Hypertension, Combination therapy

## 1. INTRODUCTION

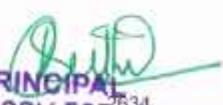
Diabetes and hypertension are common diseases of great importance and their management requires attention, both clinically and pharmacologically. Hypertension is extremely common co-morbidity in patients with type 2 diabetes mellitus. The presence of hypertension in patients with type 2 diabetes is particularly destructive because of their strong linkage with cardiovascular diseases (CVD), stroke, progression of renal disease and diabetic nephropathy [1]. Even it is very hard to control hypertension in diabetic hypertensive patients and hence antihypertensive combination therapy is required to take control over the elevated blood pressure [2]. In type II diabetics also, hypertension and diabetes are commonly associated and here obesity is the factor which could produce a spurious association [3]. Despite these possible confounding factors, most studies which have taken obesity and nephropathy into account still report a strong association between hypertension and diabetes, although this remains a controversial point [4]. In any event, a large number of patients with both hypertension and diabetes do exist. These patients have two major risk factors for cardiovascular disease and it is important, therefore, to

establish guidelines for their management. Furthermore, we now have information that controlling blood pressure in diabetics is positively beneficial as far as the progression of nephropathy is concerned. Balanced against this, however, is the problem that most available antihypertensive drugs are known to worsen glycaemic control and we have no comparative data to guide us on which drugs we should use.

## 2. MATERIALS AND METHODS

The prospective observational study was undertaken at the Inpatient department in a tertiary health care hospital, Erode, Tamil Nadu. The study was performed for a period of six months. A separate data entry form was prepared to record patient details like name, age, sex, educational status, life events, social history and prescribed drugs. After obtaining informed consent form from the patient, the demographic data like (age, gender, educational status, diagnosis and prescriptions) were collected by using a suitable data entry form. Patients with hypertension, diabetes and comorbid disease were selected. The utilization pattern of antihypertensive therapy was analyzed and also the glycemic levels of patients taking



  
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