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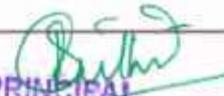
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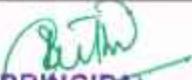
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						Link to website of the Journal	Link to article / paper / abstract of the article
1	A REVIEW ON PHARMACOKINETIC AND PHARMACODYNAMIC DRUG INTERACTIONS OF ADRENER-GIC B-BLOCKERS WITH CLINICALLY RELEVANT DRUGS-AN OVERVIEW	DR. B. Raj Kapoor	CURRENT DRUG METABOLISM	2021	1389-2002	https://benthamscience.com/public/journals/current-drug-metabolism	https://www.eurekaselect.com/article/116134
2	APPLICATION OF ARTIFICIAL INTELLIGENCE TO ADDRESS ISSUES RELATED TO THE COVID-19 VIRUS	DR. M. Senthilraja	SLAS TECHNOLOGY	2021	2472-6303	https://slas-technology.org/	https://slas-technology.org/article/s2472-6303(22)01102-5/fulltext
3	ASSOCIATION OF MEDICATION ADHERENCE WITH QUALITY OF LIFE AND TREATMENT SATISFACTION AMONG CHRONIC KIDNEY	Ms. M. Sudha	INTERNATIONAL JOURNAL OF PHARMACEUTICAL RESEARCH	2020	0975-2366	http://www.ijpronline.com/	http://www.ijpronline.com/viewarticledetail.aspx?id=18527




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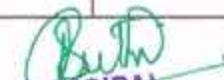
	DISEASE PATIENTS						
4	DEVELOPMENT OF QUICK REFERENCE MANUAL FOR THE MANAGEMENT OF DRUG OVERDOSE AND POISONING	DR. N. Venkateshwaramurthy	INDIAN JOURNAL OF FORENSIC MEDICINE & TOXICOLOGY	2021	0973-9122	https://www.ijfnt.com/	https://medicopublication.com/index.php/ijfnt/article/view/13509/12403
5	HMG-COA REDUCTASE INHIBITORS (STATINS) AND THEIR DRUG INTERACTIONS INVOLVING CYP ENZYMES, P-GLYCOPROTEIN AND OATP TRANSPORTERS-AN OVERVIEW(REVIEW)	DR. B. Raj Kapoor	CURRENT DRUG METABOLISM	2021	1389-2002	https://benthamscience.com/public/journals/current-drug-metabolism	https://benthamscience.com/article/113319
6	IN VITRO ANTIOXIDANT AND IN VIVO HEPATOPROTECTIVE ACTIVITIES OF ROOT BARK EXTRACT AND SOLVENT FRACTIONS OF CROTON MACROSTACHYUS HOCHST. EX DEL. (EUPHORBIACEAE) ON PARACETAMOL-INDUCED LIVER DAMAGE IN MICE	DR. B. Raj Kapoor	JOURNAL OF EXPERIMENTAL PHARMACOLOGY	2021	1179-1454	https://www.dovepress.com/journal-of-experimental-pharmacology-journal	https://www.dovepress.com/in-vitro-antioxidant-and-in-vivo-hepatoprotective-activities-of-root-bark-extract-and-solvent-fractions-of-croton-macrostachyus-hochst-ex-del-euphorbiaceae-on-paracetamol-induced-liver-damage-in-mice




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7	IN VIVO ANTITUMOR ACTIVITY OF ETHANOLIC EXTRACT OF FLEPIDAGATHIS PUNGENSNEES WHOLE PLANT	DR. S. Ananda Thangadurai	INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACEUTICAL SCIENCES	2020	0975-7538	https://iirps.com/index.php/home	https://iirps.com/index.php/home/article/view/1747/6700
8	KNOWLEDGE, ATTITUDE AND PRACTICE TOWARDS COVID-19 PANDEMIC AMONG KERALITES AND THE BARRIERS INVOLVED-AN ONLINE WEB SURVEY	DR. K. Krishnaveni	INTERNATIONAL JOURNAL OF PHARMACEUTICAL RESEARCH	2020	0975-2366	http://www.iipronline.com/	http://www.iipronline.com/viewarticledetail.aspx?id=17377
9	MECHANISTIC INSIGHTS INTO HYPERURICEMIA-ASSOCIATED RENAL ABNORMALITIES WITH SPECIAL EMPHASIS ON EPITHELIAL-TO-MESANGIAL TRANSITION: PATHOLOGIC IMPLICATIONS AND PUTATIVE PHARMACOLOGIC TARGETS	DR. P. Balakumar	PHARMACOLOGICAL RESEARCH	2020	1043-6618	https://www.sciencedirect.com/journal/pharmacological-research	https://www.sciencedirect.com/science/article/abs/pii/S1043661820315176
10	NIGELLA SATIVA (BLACK SEEDS), A POTENTIAL HERB FOR THE PHARMACEUTICAL THERAPEUTICS	DR. B. Rajkapoor	CURRENT CARDIOLOGY REVIEWS	2020	1573-403X	https://benthamscience.com/public/journals/current-cardiology-review	https://benthamscience.com/article/111339




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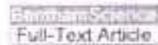
	C MANAGEMENT OF HYPERTENSION-A REVIEW						
11	PHARMACOKINETIC APPROACH OF CLINICALLY IMPORTANT DRUG INTERACTIONS OF HORMONAL CONTRACEPTIVES – A REVIEW	DR. B. Raj Kapoor	ENDOCRINE, METBOLIC AND IMMUNE DISORDERS- DRUG TARGETS	2020	1871-5303	https://www.eurekaselect.com/journal/59	https://pubmed.ncbi.nlm.nih.gov/32819252/
12	PROTECTIVE EFFECT OF CROTON MACROSTACHYUS (EUPHORBIACEAE) STEM BARK ON CYCLOPHOSPHAMIDE-INDUCED NEPHROTOXICITY IN RATS	DR. B. Raj Kapoor	JOURNAL OF EXPERIMENTAL PHARMACOLOGY	2020	1179-1454	https://www.dovepress.com/journal-of-experimental-pharmacology-journal	https://www.dovepress.com/protective-effect-of-croton-macrostachyus-euphorbiaceae-stem-bark-on-c-peer-reviewed-fulltext-article-jep
13	THE POTENTIAL MODULATORY ROLE OF CURCUMIN ON RENAL EPITHELIAL-TO-MESENCHYMAL TRANSITION IN RENAL DISEASES	DR. P. Balakumar	PHARMACOLOGICAL RESEARCH	2020	1043-6618	https://www.sciencedirect.com/journal/pharmacological-research	https://www.sciencedirect.com/science/article/abs/pii/S1043661821002309



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FULL TEXT LINKS

 Full-Text Article

Review Curr Drug Metab. 2021;22(9):672-682. doi: 10.2174/1389200222666210614112529.

A Review on Pharmacokinetic and Pharmacodynamic Drug Interactions of Adrenergic β -blockers with Clinically Relevant Drugs–An Overview

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Affiliations

PMID: 34182907 DOI: 10.2174/1389200222666210614112529

Abstract

Adrenergic β -blockers are used to treat many conditions, including hypertension, cardiac arrhythmias, heart failure, angina pectoris, migraine, and tremors. The majority of the β -blockers including Propranolol, Metoprolol, Acebutolol, Alprenolol, Betaxolol, Carvedilol, Nebivolol and Oxprenolol are metabolised majorly by CYP2D6, and Bisoprolol is primarily metabolised by CYP3A4 enzymes. The drugs inhibiting or inducing them may alter the pharmacokinetics of those β -blockers. The plasma concentrations of Propranolol might be elevated by the concomitant use of drugs, such as SSRIs (Fluoxetine, Paroxetine), SNRIs (Duloxetine) and Cimetidine, while the plasma concentrations of Metoprolol increased by the concurrent use of SSRIs (Fluoxetine, Paroxetine), Amiodarone, Celecoxib, Cimetidine, Terbinafine, and Diphenhydramine. β -blockers can also interact pharmacodynamically with drugs, including fluoroquinolones, antidiabetic agents and NSAIDs. In addition, β -blockers may interact with herbs, such as curcumin, Ginkgo bifoba, Schisandra chinensis, green tea, guggul, hawthorn, St. John's wort and Yohimbine. This article focuses on clinically relevant drug interactions of β -blockers with commonly prescribed medications. In addition to Pharmacokinetics and Pharmacodynamics of the drug interactions, recommendations for clinical practice are highlighted. The prescribers and the pharmacists are needed to be aware of the drugs interacting with β -blockers to prevent possible adverse drug interactions.

Keywords: CYP2D6 enzyme; CYP3A4 enzyme; Drug interactions; adrenergic β -blockers; pharmacodynamic interactions; pharmacokinetic interactions

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Application of Artificial Intelligence to Address Issues Related to the COVID-19 Virus

SLAS Technology
2021, Vol. 26(2) 123–126
© Society for Laboratory
Automation and Screening 2021
DOI: 10.1177/2472630320983813
journals.sagepub.com/home/jla
SAGE

M. Senthilraja¹

Abstract

Artificial intelligence (AI) plays a major role in addressing novel coronavirus 2019 (COVID-19)-related issues and is also used in computer-aided synthesis planning (CASP). AI, including machine learning, is used by artificial neural networks such as deep neural networks and recurrent networks. AI has been used in activity predictions like physicochemical properties. Machine learning in de novo design explores the generation of fruitful, biologically active molecules toward expected or finished products. Several examples establish the strength of machine learning or AI in this field. AI techniques can significantly improve treatment consistency and decision making by developing useful algorithms. AI is helpful not only in the treatment of COVID-19-infected patients but also for their proper health monitoring. It can track the crisis of COVID-19 at different scales, such as medical, molecular, and epidemiological applications. It is also helpful to facilitate the research on this virus by analyzing the available data. AI can help in developing proper treatment regimens, prevention strategies, and drug and vaccine development. Combination with synthesis planning and ease of synthesis are feasible, and more and more automated drug discovery by computers is expected in the near future to eradicate the COVID-19 virus.

Keywords

COVID-19, artificial intelligence, virus, machine learning, applications

Introduction

Amid the worldwide health crisis, the medical discipline is looking for new technologies to monitor and control the spread of the novel coronavirus 2019 (COVID-19) pandemic infection. Artificial intelligence (AI) is one such technology that can easily track the spread of this virus; it identifies the high-risk patients and is useful in controlling this infection in real time. It can also predict the mortality risk by adequately analyzing the previous data of the patients. AI can help us to fight this virus via patient screening, medical checkups and help, notifications, and suggestions about infection control.^{1–3} This technology has the potential to improve the planning, treatment, and reported outcomes of the COVID-19 patient, being an evidence-based medical tool. **Figure 1** shows the general procedure of AI-based applications that help medical practitioners identify COVID-19 symptoms.

Figure 1 summarizes the testing, screening, and monitoring of suspected cases, which lead to minimizing virus infection, by AI, including machine learning–based treatment.^{4–6} There are significant steps of treatment that include high accuracy and reduce the complexity and time taken when using an AI method. Medical and paramedical professionals are not only focused on treatment of the patient but also involved in the control of disease with applications of AI.

These test analyses were done based on the major symptoms that occurred or were observed by machine learning techniques, which have the highest-accuracy prediction and minimize the long time previously taken during the whole process, making these techniques more usable in the future.^{7–8}

Major Applications of Artificial Intelligence in COVID-19 Pandemic Conditions

Actual and Potential Contributions of Artificial Intelligence against COVID-19

AI can contribute to the fight against COVID-19 in six areas: (1) early warnings and alerts, (2) tracking and prediction, (3) data dashboards, (4) diagnosis and prognosis, (5) treatments and cures, and (6) social control.

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Received Jul 8, 2020, and in revised form Nov 16, 2020. Accepted for publication Nov 24, 2020.

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Article Detail

Association of Medication Adherence with Quality of Life and Treatment Satisfaction Among Chronic Kidney Disease Patients

Author: . ALEENA ANDREW, SARA JOSE, SUDHA M, VENKATESWARAMURTHY N, SAMBATH KLIMAR R, SHANMUGASUNDARAM R.

Abstract: Chronic kidney disease is a global public health problem due to the rapid rise of common risk factors such as diabetes and hypertension. Patients with CKD are prescribed a regime of multi pharmacological treatment. This study was conducted in a secondary care hospital in South India to study the association of medication adherence with quality of life and treatment satisfaction among Chronic Kidney Disease patients (CKD). **Methods:** A prospective observational study was conducted for a period of six months in a secondary care hospital. 142 CKD patients on medications for more than 6 months were included. The patients medication adherence, quality of life and treatment satisfaction were assessed using self reported questionnaires. **Results:** Out of 142 CKD patients 100 (70.42%) were males and 42 (29.57%) were females. The majority of patients were in the age group of 51-60 years (36%). The rate of medication adherence was low (53.30%) in majority of the CKD patients. The quality of life and treatment satisfaction was found to be low in non adherent CKD patients. **Conclusion:** Medication adherence was found to be low in majority of CKD patients. This low adherence may be due to several factors like age, gender, social habits, comorbidities, educational status etc. The quality of life and treatment satisfaction comparatively decreased in CKD patients who were nonadherent to medication.

Keyword: Chronic kidney disease; Medication adherence; Quality of life; Treatment Satisfaction

DOI: <https://doi.org/10.31838/ijpr/2021.13.01.165>

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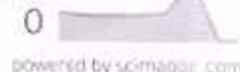
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Development of Quick Reference Manual for the Management of Drug Overdose and Poisoning

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Abstract

Aim: To develop a reference manual for the management of drug overdose and poisoning.

Methods: A prospective developmental study was performed for a span of six months at a tertiary care hospital in Erode. Information on the management of cases of drug overdose and poisoning was provided based on queries received at the Drug Information Center and the poisoning cases identified in the respective hospital over the past three years. Further attention was paid to detecting local poisons. Such information was collected on the basis of literature reviews, magazines and newspapers. In addition to drug and poison monographs; android applications, toxicological databases and links, standard reference books and articles on drug overdose and poisoning were included. Locally reported cases have been given more focus.

Results: A formulary was prepared which includes the management information for 100 drugs and 57 toxic substances that were identified after extensive research. The signs and symptoms of the various poisoning cases were graded as mild, moderate and severe based on poison severity scale (PSS) and respective antidotes were mentioned.

Conclusion: As per our knowledge, this is the first formulary that focus on local poisons. The implementation of the formulary may have a significant impact on healthcare professionals to improve the quality of life of patients. This provides important information of localized poisoning and drug overdose in a nutshell and therefore offers as a quick data to the enquirer.

Key words: Drug overdose, Formulary, Monograph, Poisoning

Introduction

Poisoning and drug overdose are important health problems in developing countries.¹ The WHO reports annually that 0.3 million people are killed by specific poisoning agents. Acute pesticide poisoning is one of the most common causes of intentional death worldwide.² High doses of analgesics, tranquilizers and antidepressants are widely used for intentional poisoning in industrialized countries and agricultural pesticides are used in Asia for self-poisoning, especially in rural areas with a fatality range of 10-20 percent.^{3,4}

Almost a million people die each year as a result of suicide, and chemicals account for a significant number of these deaths. An estimated 370,000 deaths each year

are caused by deliberate ingestion of pesticides.⁵ On average, because of an accidental drug overdose, India loses at least two people every day. According to the latest data released by the Ministry of Health and Family Welfare, in three years from January 2014 to January 2016, 2381 people died from drug overdose, with 5 states responsible for 53% of all cases. Tamil Nadu peaks at 20%, followed by Punjab with 15%.

In India, especially in southern India, the incidence of drug overdose poisoning, organophosphates, and plant poisoning is growing. Tamil Nadu is topping deaths because of a drug overdose, according to the National Crime Records Bureau.^{6,7}




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HMG-CoA Reductase Inhibitors (Statins) and their Drug Interactions Involving CYP Enzymes, P-glycoprotein and OATP Transporters-An Overview

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Abstract: Background: Hydroxymethyl glutaryl-CoA (HMG-CoA) reductase inhibitors (Statins) are used to treat dyslipidemia. Generally, the statins are the substrates of CYP enzymes, P-glycoprotein (P-gp), and organic anion transporting polypeptides transporters (OATP1B1).

Objective: This review article focuses on the clinical significance of statins, and their interactions in real practice.

Methods: The databases like Medline/PubMed Central/PubMed, Google Scholar, Science Direct, Cochrane Library, Directory of open access journals (DOAJ), and reference lists were searched to identify relevant articles.

Results: Most of the drug interactions of statins result in elevated plasma concentrations and toxicity of statins due to the inhibition of CYP3A4, P-gp and/or OATP1B1 transporters. The toxicity of statins includes myopathy, rhabdomyolysis, elevated liver enzymes, acute kidney injury, and diabetes. The statins like simvastatin, lovastatin, and atorvastatin are substrates of CYP3A4 enzyme and P-glycoprotein and their concomitant use with the drugs inhibiting or inducing them would result in changes in plasma concentrations and toxicity/efficacy. However, the statins like pravastatin, rosuvastatin and pitavastatin are not substrates of CYP enzymes and hence the concomitant use of CYP inhibitors or inducers does not affect them. Almost all the statins are the substrates of OATP1B1 transporter, and the co-prescription of inhibitors of OATP1B1 elevates the plasma concentrations and muscle toxicity of statins.

Conclusion: Understanding the interacting potential of each statin will enable the prescribers, pharmacists, and other health care professionals to use statins effectively without compromising patient safety.

Keywords: Drug interactions, statin, HMG-CoA reductase inhibitors, CYP3A4, P-glycoprotein, OATP1B1 transporter.

ARTICLE HISTORY

Received: July 29, 2020
Revised: November 21, 2020
Accepted: November 25, 2020

DOI:
10.2174/1589200222066210114122729



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1. INTRODUCTION

Hydroxymethylglutaryl-CoA (HMG-CoA) reductase inhibitors (Statins) decrease the morbidity and mortality in patients with dyslipidemia by lowering the plasma concentrations of total cholesterol, low-density lipoprotein (LDL), and triglycerides while elevating high-density lipoprotein (HDL) concentrations [1]. They are primarily recommended in the treatment of atherosclerosis and the prophylaxis of myocardial infarction, and stroke [2].

Statins reduce hepatic cholesterol syntheses by inhibiting the Hydroxymethylglutaryl-CoA (HMG-CoA) reductase enzyme responsible for the conversion of HMG-CoA to mevalonate [3]. The toxicity of statins associated with the adverse effects includes myopathy [4, 5], rhabdomyolysis [6], elevated liver enzymes [7], acute kidney injury and diabetes [8-10]. The symptoms of statin-induced myopathy include muscle pain, muscle tenderness, muscle weakness, fatigue, and cramping.

Statins are the substrates of cytochrome P450 (CYP) enzymes, P-glycoprotein (P-gp) and Organic anion transporting polypeptides (OATPs) transporters, generally. The lipophilic statins such as simvastatin, lovastatin, and atorvastatin primarily depend on the CYP3A4 enzyme for their metabolism [11] while the metabolism of Fluvastatin is done mainly by the CYP2C9 isoenzyme [12]. The

hydrophilic statins like rosuvastatin [13, 14] and pravastatin [15] are not significantly affected by CYP-mediated metabolism and excreted in unchanged form.

The statins like atorvastatin, lovastatin, pitavastatin, and simvastatin have been identified as the substrates and inhibitors of P-gp transporters [16, 17]. The substrates and inhibitors of P-gp transporter are also known to have overlapping substrate specificity to CYP3A enzymes [18].

All statins are the substrates of OATP1B1 transporter. In addition, the statins such as pravastatin and atorvastatin are found to be the substrates of OATP2B1 and Pitavastatin, a substrate of OATP1B3, while fluvastatin and rosuvastatin as the substrates of OATP1B3 and OATP2B1 [19].

Patients with many comorbid conditions may take multiple medications which may result in polypharmacy and the risk of drug interaction is increased with the number of comedICATIONS [20]. This review article focuses to explore the clinical significance of the specific interaction between statins and other drugs and to provide recommendations on how to deal with such interactions to minimize risks and ensure effective statin doses. This might be beneficial for the prescribers and health care professionals to understand effectively without compromising the patient's safety.

2. METHODS

In this review, relevant articles were searched within the databases like as Medline/PubMed Central/PubMed, Google Scho-

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In vitro Antioxidant and in vivo Hepatoprotective Activities of Root Bark Extract and Solvent Fractions of *Croton macrostachyus* Hochst. Ex Del. (*Euphorbiaceae*) on Paracetamol-Induced Liver Damage in Mice

This article was published in the following Dove Press journal:
Journal of Experimental Pharmacology

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Background: Liver disease is a major public health threat, particularly in developing countries. Several medicinal plants and formulations have been claimed to have liver protective activities. The present study aimed to evaluate in vitro antioxidant and in vivo hepatoprotective activities of root bark extracts of *Croton macrostachyus* (*Euphorbiaceae*).

Methods: Free radical scavenging activity of crude extract and solvent fractions of the plant was conducted using the DPPH assay method. Hepatoprotective activities of the crude extract and solvent fractions of the plant were carried out based on paracetamol-induced liver damage in mice. Serum biomarkers (AST, ALT, ALP, total bilirubin and total protein) were assessed to find out the effect. Histopathological examination was also carried out for all groups of mice to further confirm the findings.

Results: Antioxidant assay revealed that the crude extract, aqueous fraction and chloroform fraction of *Croton macrostachyus* exhibited free radical scavenging activity with IC₅₀ values of 128.6, 168.9, and 406 µg/mL, respectively. Pretreatment of the mice with the crude extract and solvent fractions of *Croton macrostachyus* significantly reduced ALP (p<0.001), ALT (p<0.001), and AST (p<0.001) levels at all the administered doses compared to the toxic group. The crude extract and chloroform fraction decreased total bilirubin level at doses of 200 mg/kg (P<0.05) and 400 mg/kg (P<0.001). Pretreatment of the mice with 400 mg/kg of the crude extract and aqueous fraction elevated total protein value compared to the paracetamol treated group (P<0.05). The hepatoprotective activities of the plant extracts were confirmed by histopathological studies.

Conclusion: From this study, it can be concluded that the crude extract and solvent fractions of *Croton macrostachyus* demonstrated antioxidant and hepatoprotective activities.

Keywords: antioxidant, hepatoprotective, *Croton macrostachyus*, paracetamol, biochemical parameters, liver damage

Background

Liver diseases are among the global health problems; In which, liver cirrhosis is the ninth leading cause of death in western Nations.¹ Toxic chemicals, xenobiotics, alcohol consumption, malnutrition, anemia, medications, autoimmune disorders, and viral infections^{2,3} are some major causes of liver disease; among which,

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In Vivo Antitumor Activity of Ethanolic Extract of *Lepidagathis Pungens* Nees Whole Plant

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Article History:

Received on: 01 Oct 2020
 Revised on: 01 Nov 2020
 Accepted on: 04 Nov 2020

Keywords:

anti-tumour,
 Lepidagathis,
 EAC method,
 dose dependence

ABSTRACT

Cancer is the most dreadful of all the diseases and is the major contributors to the mortality in the world. Out of all the population, almost 1.2 million patients die due to cancer and related problems. The rate and spread of cancer are wide and even in both women and men. It is presently as high as 3.5 million people who have cancer in India alone. There are many ways of treatment of cancer like the surgery, radiation therapy, cryosurgery and chemotherapy. A part of chemotherapy is the usage of a lot of chemicals and synthetic drugs. Due to the side effects of chemotherapy, patients often get symptoms due to the usage of drugs, and so the cancer treatment often is toxic. Because of this, herbal drugs are seemed to have no side effects, and non-toxic effects, and so this project deals with identifying the plant sources of the drugs that treat cancers effectively. The present study focusses on the extraction of the chemical constituents from *Lepidagathis pungens* whole plant and using the same to estimate the anti-tumour potential in EAC induced tumour induction method. The activity was tested in two doses 200 and 400 mg/kg of the extract. They showed a dose-dependent activity when estimated for the tumour parameters and other haematological measures like RBC, WBC counts. They showed similar activity when estimated for the antioxidant enzymes like SGOT, SGPT, Catalases, LPO and ALP levels.

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ISSN: 0975-7538

DOI: <https://doi.org/10.26452/ijrps.v11i4.3614>

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INTRODUCTION

Cancer is the most dreadful of all the diseases and is the major contributors to the mortality in the world.

Out of all the population, almost 1.2 million patients die due to cancer and related problems. The rate and spread of cancer are vast, and even in both women and men. It is presently as high as 3.5 million people who have cancer in India alone (Shrikhande *et al.*, 2007).

It is estimated that the growth of the cancer is caused by benign polyps and other growths in the organs of the body. An estimate is there up to 2/3 cases of the polyps turn into cancers which are malignant (World Health Organization, 2008). There are often no symptoms of cancers in the initial stages, and they may spread to other parts of the body which causes malignancy. Symptoms start when the cancers grow to a more severe stage, usu-



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Pharmacological Research

Volume 161, November 2020, 105209

Mechanistic insights into hyperuricemia-associated renal abnormalities with special emphasis on epithelial-to-mesenchymal transition: Pathologic implications and putative pharmacologic targets

Pitchai Balakumar,^{a,1} Ali Alqahtani,^b Noohu Abdulla Khan,^c Nanjajan Mahadevan,^d Sockalingam A. Dhanaraj,^e

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Abstract

Though the pathogenesis of hyperuricemia-induced renal complications is not precisely known, **hyperuricemia** has been recognized as an independent risk factor for renal disease. While the clinical implication of **hyperuricemia** in renal disease has been a contemporary topic of debate, growing body of bench and clinical evidences certainly suggest a causative role of high **uric acid** in renal abnormalities by implicating diverse pathologic and molecular mechanisms. **Urate** crystals after having deposited in the kidney could cause hyperuricemia nephropathy leading to **glomerular hypertrophy** and tubulointerstitial **fibrosis**, while high serum **uric acid** might predict progressive **renal damage** and dysfunction. Hyperuricemia could be associated with manifestation of tubular injury and macrophage infiltration as well as an increased expression of inflammatory mediators. This review sheds light on the mechanistic aspects pertaining to hyperuricemia-associated renal abnormalities. Besides, the renal detrimental actions of high uric acid possibly mediated through its potential role on oxidative stress, **renal inflammation**, **endothelial dysfunction**, glycocalyx shedding, endothelial-to-mesenchymal transition and more specifically on the renal epithelial-to-mesenchymal transition have been addressed. Moreover, this review discusses a number of potential targets such as endothelin-1, TLR4/NF- κ B, PI3K/p-Akt, Wnt5a/Ror2, NLRP3 **inflammasome**, **NADPH oxidase**, ERK1/2, **enhancer of zeste homolog 2**, **serum response factor** and Smad3/TGF- β signalling pathways, among others, implicated in hyperuricemia-associated renal abnormalities. This review finally appraises a number of bench and clinical studies which supporting a notion that the pharmacologic reduction of high uric acid might have a therapeutic value in the management of renal abnormalities, with an emphasis on **febuxostat** and its renal pleiotropic actions.

Graphical abstract

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MINI-REVIEW ARTICLE

***Nigella Sativa* (Black Seeds), A Potential Herb for the Pharmacotherapeutic Management of Hypertension : A Review**Naina M.P. Maideen^{1*}, Rajkapoor Balasubramanian² and Sambathkumar Ramanathan²¹Department of Clinical Pharmacy, Dubai Health Authority, P.O Box: 4545, Dubai, United Arab Emirates; ²Department of Pharmacology, J.K.K. Nattraja College of Pharmacy, Komarapalayam 638 183, India

ARTICLE HISTORY

Received: July 20, 2020

Revised: September 15, 2020

Accepted: September 18, 2020

DOI:

10.2174/1373401X16666201110125005

Abstract: Hypertension is one of the leading risk factors for stroke, myocardial infarction and untimely death. The prevalence of hypertension is extremely high among the global population, and many of them depend on modern medicines to manage their blood pressure. The modern antihypertensive medications include angiotensin-converting enzyme inhibitors (ACEIs), angiotensin II receptor blockers (ARBs), calcium channel blockers (CCBs), diuretics, beta-adrenergic blockers, direct renin inhibitors, direct-acting vasodilators, alpha-adrenergic blockers and centrally acting drugs that are associated with many harmful and undesirable effects. The patients may consider traditional herbal medicines as a good strategy to manage chronic conditions due to the reasons such as perceived failure of allopathic medicines, relatively high cost of allopathic medicines, social-cultural practices and/or herbal knowledge, poor access to medical facilities and safety concerns about modern medicines. *Nigella sativa* (Black seeds) has been used to treat various conditions, including hypertension, obesity, diabetes, cancer, etc. Hence, the antihypertensive potential of *N. sativa* is analyzed in this review. The literature was searched in databases including Medline/PMC/PubMed, Google Scholar, ScienceDirect, Directory of Open Access Journals (DOAJ) and reference lists to identify articles associated with antihypertensive properties of *N. sativa*. Numerous randomized controlled trials and animal studies reported that *N. sativa* has potential antihypertensive effects. Hence, *N. sativa* could be used effectively to manage patients with stage 1 hypertension, and the patients using modern antihypertensive medications could reduce their doses by adding *N. sativa* into their regimen as adjuvant therapy.

Keywords: *Nigella sativa*, black seeds, kalonji, hypertension, thymoquinone, thymol, nigellone.

1. INTRODUCTION

Hypertension or high blood pressure is considered globally as an important risk factor for cardiovascular diseases, including myocardial infarction, stroke and premature death [1]. Blood pressure is the product of peripheral vascular resistance (PVR), and cardiac output (CO) is the product of stroke volume (SV) and heart rate (HR). Hence, the blood pressure could be modified by the factors affecting PVR, SV and/or HR [2]. Hypertension may occur due to various factors, including up-regulation of renin-angiotensin-aldosterone-system (RAAS), overactive sympathetic system, increased peripheral vascular resistance, psycho-emotional stress, oxidative stress, endothelial dysfunction, and some genetic factors [3].

The incidence of hypertension among the global population has been estimated as 972 million (26%) in 2000 [4] and 1.13 billion in 2015 [5]. Moreover, adults living in low and middle-income countries had more prevalence of hypertension (1.04 billion) than those from high-income countries (349 million) [6].

The modern antihypertensive medications include angiotensin-converting enzyme inhibitors (ACEIs), angiotensin II receptor blockers (ARBs), calcium channel blockers (CCBs), diuretics, beta-adrenergic blockers, direct renin inhibitors, direct-acting vasodilators, alpha-adrenergic blockers and centrally acting drugs [7] and the first-line antihypertensive drugs include ACEIs, ARBs, CCBs, or thiazide diuretics as per the recommendation from the eighth joint national committee (JNC 8) and American college of cardiology/American heart association task force [8].

The use of herbal medicine to manage chronic conditions such as hypertension, diabetes, etc., is popular among the global population as modern medicines are associated with many harmful and undesirable side effects [9]. Moreover, the patients may consider traditional herbal medicines as a good strategy to manage chronic conditions due to the reasons such as perceived failure of allopathic medicines, relatively high cost of allopathic medicines, social-cultural practices and/or herbal knowledge, poor accessibility to medical facilities and safety concerns about allopathic medicines [10].

Nigella sativa (Black seeds or Black cumin seeds) is a miracle herb, and it has been used to treat various conditions, including hypertension, obesity, diabetes, cancer, etc [11]. Above all, Prophet Muhammad (PBUH) stated that "In

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Pharmacokinetic Approach of Clinically Important Drug Interactions of Hormonal Contraceptives – A Review

Author(s): [Nagesh M.K. Madhavi](#), [Sankaranarayanan Sankaranarayanan](#) and [Sankaranarayanan Sankaranarayanan](#)

Volume 21, Issue 7, 2021

Published on: 20 August, 2020

Page: [1219 - 1231]

Pages: 13

DOI: [10.1080/10715393.2020.1849371](https://doi.org/10.1080/10715393.2020.1849371)

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Abstract

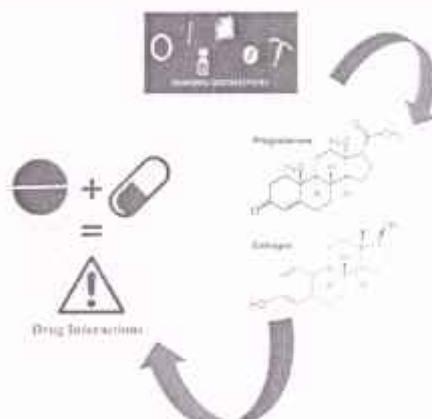
Hormonal contraceptives contain an Estrogen and/or a Progestin, which are the substrates of the CYP3A4 enzyme and the drugs inducing the CYP3A4 enzyme can decrease the plasma concentrations and thereby therapeutic efficacy of Hormonal contraceptives resulting in unintended pregnancy. Moreover, the hormonal contraceptives associated risk of thrombotic events are further exacerbated by the simultaneous administration of drugs like Tranexamic acid and tobacco smoke. Therefore, while prescribing hormonal contraception and other drugs to women, drug interactions should always be considered because there could be a possible contraceptive failure or other adverse drug effects. This article provides a summary of guidance to healthcare professionals such as prescribers and pharmacists on pharmacokinetic based interactions between hormonal contraception and other drugs.

Keywords: Drug interactions, hormonal contraceptives, ethinyl estradiol, levonorgestrel, pharmacokinetic interactions, pharmacodynamic interactions.

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Graphical Abstract



Estrogen and/or a Progestin, which are the substrates of CYP3A4 enzyme and the drugs inducing CYP3A4 enzyme, can decrease the plasma concentrations and therapeutic efficacy of hormonal contraceptives.

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Protective Effect of *Croton macrostachyus* (Euphorbiaceae) Stem Bark on Cyclophosphamide-Induced Nephrotoxicity in Rats

This article was published in the following Dove Press journal:
Journal of Experimental Pharmacology

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Dawit Zewdu Wondafrash¹
Abera Hadgu Berhe¹

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Background: Cyclophosphamide is an alkylating antineoplastic agent and its major limitation is injury to normal tissue, leading to multiple organ toxicity, including kidney, heart, liver and reproductive toxicity. *Croton macrostachyus* (Euphorbiaceae) has been used in Ethiopian traditional medicine to manage renal diseases.

Objective: The present study aims to assess the protective effect of the stem bark extract and solvent fractions of *Croton macrostachyus* on cyclophosphamide-induced nephrotoxicity in rats.

Methods: Nephrotoxicity was induced using cyclophosphamide 200 mg/kg i.p injection on the first day of the experiment. The negative control groups were administered with cyclophosphamide alone (200 mg/kg, i.p.). The crude extracts were administered at three dose levels (100, 200, and 400 mg/kg), while aqueous and ethyl acetate fractions were given at two dose levels (100 and 200 mg/kg). Excepting the normal control, all groups were subjected to cyclophosphamide toxicity on the first day.

Results: Treatment with crude extract 100 mg/kg and ethyl acetate fraction significantly decreased kidney-to-body weight ratio ($P < 0.001$). In addition, treatment with *Croton macrostachyus* crude extract and solvent fractions significantly decreased serum blood urea nitrogen (BUN) level ($P < 0.001$). Treatment with 100 and 200 mg/kg of ethyl acetate fraction significantly decreased serum creatinine level. Histopathological results confirmed the protective effect of the crude extract and solvent fractions of *Croton macrostachyus*.

Conclusion: *Croton macrostachyus* possesses nephroprotective activities and it could be a possible source of treatment for cyclophosphamide-induced nephrotoxicity.

Keywords: *Croton macrostachyus*, cyclophosphamide, nephrotoxicity, creatinine, blood urea nitrogen

Introduction

Drug-induced kidney damage is not a surprising effect since 25% cardiac output goes to the kidney, which puts kidney at increased exposure to the administered medications.¹ Anticancer drugs, aminoglycoside antibiotics, conventional non-selective non-steroidal anti-inflammatory drugs and amphotericin B are well known to cause renal damage.^{2,3}

Renal damage is a challenging adverse effect that can hinder the clinical use of antineoplastic drugs.⁴ Nephrotoxicity reflects both tubular and glomerular injuries and which will result in acute or chronic functional alterations. According to reports, the frequency of drug-induced nephrotoxicity is around 14–26% in adult populations;

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Letter to the Editor

The potential modulatory role of curcumin on renal epithelial-to-mesenchymal transition in renal diseases



Dear Editor,

The epithelial-to-mesenchymal transition (EMT) is an intricate and multifaceted series of coordinated event wherein the epithelial cells progressively undergo a specific biochemical changes and subsequently get transition into the mesenchymal-like cells, gradually losing their epithelial features. A growing body of bench evidence suggests that EMT plays a key role in the pathogenesis of renal abnormalities, especially in renal fibrosis. Tubulointerstitial fibrosis is considered a final common pathway in the end-stage renal disease, while EMT has been suggested to be an important contributor to tubulointerstitial fibrosis by augmenting the number of myofibroblasts [1]. Despite the exploration and identification of several key molecular signaling mechanisms involved in the regulation of renal EMT, this particular pathologic event seems to have no specific treatment. Identification and characterization of potential pharmacologic interventions that modulate the pathologic event of renal EMT and its deleterious renal outcomes may be of great importance in the management of associated renal abnormalities. Curcumin exhibits a protective effect against the development of experimental renal fibrosis in animal models; nevertheless, the underlying key mechanisms and molecular cellular signaling involved in this context are not precisely understood. Interestingly, recent bench studies have reported an emerging role of curcumin in the amelioration of renal EMT and associated renal abnormalities through modulation of a number of important molecular signal transduction pathways [2–4]. Herein we analyze these studies shedding light on the actual role of curcumin on renal EMT, how it acts at the molecular level, and the potential new therapeutic avenues exploiting curcumin-mediated effects on renal EMT. This article specifically describes curcumin-mediated modulatory effects on renal EMT and associated renal abnormalities. Moreover, this article provides the scientific basis for further research in distinctly understanding the ameliorative role of curcumin on renal EMT and accompanying mechanistic insights.

A fleeting look on the intricate event of EMT: The exact percentage of fibroblasts that are derived from the tubular epithelial cells in a diseased kidney is uncertain and under debate [5]. In several bench studies, EMT of tubular epithelial cells has been suggested as an important pathologic mechanism that could promote renal fibrosis. EMT may be defined as the complex cellular process in which the injured renal tubular epithelial cells could undergo a phenotype change, acquiring the mesenchymal characteristics and transforming into fibroblasts [6]. During the process of EMT, the injured epithelial cells are known to be activated and subsequently go through a phenotypic conversion, acquiring the characteristics of myofibroblasts [7]. The key events in the course of EMT process might include (a) dissolution of epithelial cell junctions and the loss of cell polarity, (b) downregulation of epithelial proteins expression including E-cadherin, and upregulation of mesenchymal markers

expression such as α -smooth muscle actin (α -SMA), vimentin and fibronectin, among others, and (c) the reorganization of cytoskeletal architecture and the changes in cell morphology along with an increased cell protrusion and motility [8]. A number of experimental evidence advocates that EMT plays an imperative role in the progression of renal tubulointerstitial fibrosis, a common pathologic mechanism leading to end-stage renal failure.

Role of curcumin on renal EMT and exploration of putative signaling mechanisms: Curcumin is known as a polyphenolic compound that is derived from rhizomes of *Curcuma*, and is shown to possess a potent antifibrotic properties [9]. Of note, Li et al. [10] found that curcumin was able to inhibit the EMT as assessed by reduced α -SMA expression and increased E-cadherin level in TGF- β 1 treated proximal tubular epithelial HK-2 cells. In this study, curcumin had counteracted TGF- β 1-induced EMT in renal tubular epithelial cells through the ERK-dependent and then the PPAR γ -dependent pathways [10]. In a subsequent study, while EMT has been recognized to play an important role in the pathogenesis of diabetic nephropathy, Sun et al. [11] suggested that curcumin did prevent the EMT of podocytes, proteinuria and kidney injury in experimental diabetic nephropathy by suppressing the phosphorylation of caveolin-1 and increasing the stabilization of caveolin-1 and β -catenin, and therefore, curcumin has a potential to ameliorate the EMT of podocytes by regulating caveolin-1 [11].

A recent experimental study by Tu et al. [12] demonstrated that curcumin did alleviate diabetic nephropathy by inhibiting the podocyte mesenchymal transdifferentiation and inducing autophagy in rats and MPC5 cells (cultured mouse podocytes). In the same study, curcumin was noted to upregulate the expression of E-cadherin and downregulate the levels of vimentin, p-mTOR, p-Akt and PI3K in diabetic nephropathy rats and MPC5 cells [12], providing the mechanistic insights pertaining to the protection offered by curcumin against the development of diabetic nephropathy. The key modulatory role of curcumin on the Akt/mTOR pathway has also been demonstrated in a study by Zhu et al. [13] in which curcumin suppressed the EMT of renal tubular epithelial cells through inhibition of the Akt/mTOR pathway. In this study, curcumin was noted to maintain the epithelial morphology, decreased expression of vimentin and α -SMA (normally induced by TGF- β 1) and increased expression of E-cadherin [13]. Furthermore, curcumin did reduce the Akt, mTOR and P70S6K phosphorylation, effectively suppressing the activity of Akt/mTOR pathway, and thus, it was suggested that curcumin antagonized TGF- β 1-driven EMT through inhibition of the Akt/mTOR pathway activity [13].

Renal interstitial fibrosis has been suggested to be associated with EMT and the accumulation of inflammatory cytokines [3]. Given the antioxidative, antifibrogenic, anti-inflammatory and antiproliferative effects of curcumin, Wang et al. [14] in their recent experimental study

<https://doi.org/10.1016/j.phrs.2021.105646>

Received 24 April 2021; Accepted 26 April 2021

Available online 9 May 2021

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Drug Induced Cognitive Impairment

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Abstract:

As a result of taking drugs, elderly patients are more likely than younger patients to acquire cognitive impairment. Drug-induced cognitive impairment is a major cause of delirium and a common complicating factor in dementia diagnosis. Age, brain disease, and addiction to alcohol and/or drugs are all risk factors for delirium. The elderly are highly susceptible due to impaired renal and liver functions associated with multiple diseases, multiple drug use, and age-related pharmacokinetic and pharmacodynamic changes. Drugs have a negative effect on cognitive functions due to the following pathophysiological mechanisms: a decrease in neuronal excitability, an increase in gamma-aminobutyric acid activity, and decreases in enzyme activity, the number of receptors, cerebral perfusion, and brain atrophy; additionally, a number of mechanisms have not been thoroughly studied. Dementia and delirium can be caused by psychoactive drugs, antidepressants, and anticonvulsants. Nonpsychoactive pharmaceuticals including histamine H2 receptor antagonists and cardiac treatments can also produce acute or persistent cognitive problems. The risk of drug-induced impairment can be reduced by implementing strategies that improve overall health, avoiding unnecessary medications, and selecting medications that are less likely to cause delirium.

Keywords: Cognitive impairment, Dementia, Delirium, Elderly patients

I. INTRODUCTION:

When a person has problems in recalling, acquiring new knowledge, concentrating, or making judgments that influence their everyday lives, they are said to have cognitive impairment. Cognitive impairment can range from mild to severe, with mild impairment referring to when people perceive changes in cognitive functioning but are still able to go about their daily lives. The ability to understand the meaning or importance of things, as well as the ability to talk and write, is lost in severe impairment, resulting in the inability to live independently.^[1]

According to estimations, the population of those over 60 years old in India will have risen from 7.7% in 2001 to 12.30% by 2025, with nearly 150 million aged people in the country.^[2] Dementia, commonly known as cognitive impairment, is a rather prevalent illness among the elderly. The majority of people with cognitive disabilities live in countries with a low and moderate income (60 percent in 2001, expected to rise to 71 percent by 2040); India's rate of increase in cognitive disability over the decades is expected that the figure will be around 300 percent, compared to only 100 percent in high-income countries.^[3] In the majority of cases, a neurologically degenerative condition is the root reason for significant cognitive decline.^[4]

Between normal ageing and dementia, there is a stage in the ageing process known as cognitive impairment. It describes a clinical scenario in which a person has memory complaints and objective evidence of cognitive impairment but no indication of dementia.^[5] Although cognitive impairment is frequent in later age and may be related to the natural process of ageing, Alzheimer's disease (AD) neuropathological changes begin in the brain in the fifth decade of life, years before clinical symptoms appear.^[6]

After the age of 60, the prevalence of dementia doubles every 5 years.^[7] In the year 2000, India had 3.5 million Alzheimer's disease/dementia patients, compared to 4.5

million in the United States (USA).^[8] The most common type of dementia is Alzheimer's disease, which is defined as an acquired cognitive and behavioural impairment severe enough to significantly restrict social and occupational functioning.^[9]

One of the most frequent reversible and preventable consequences linked with acute and chronic alterations in cognition is drug-induced cognitive impairment. In vulnerable patients, most drugs can cause some level of cognitive impairment or problems; however, particular medication types are more frequently implicated.^[10] Drug-induced cognitive impairment is more common in some groups. Confusion, delirium, and dementia are all substantial risk factors for advanced age, cognitive impairment, and dementia.^[11] The aetiology of drug-induced cognitive impairment is frequently complex. Age and sickness are known to cause changes in pharmacokinetics, pharmacodynamics, brain homeostasis, blood-brain barrier permeability, and neurochemistry.^[12,13] Additionally, an increased number of comorbidities, frailty, concomitant cognitive impairment, high pill burden, and supratherapeutic pharmaceutical serum concentrations, such as digoxin, have all been identified as key factors in predisposing an individual to drug-induced cognitive impairment.^[14] Because drug-induced cognitive impairment is frequently reversible, it is critical to perform a full medication reconciliation to ensure that the offending substance is identified and removed as soon as possible (s). Furthermore, preventative efforts such as avoiding high-risk drugs wherever possible, particularly in the most vulnerable, and/or appropriately adjusting doses based on age or pathophysiology-related changes, as well as regular follow-up and monitoring, may help to avoid issues.^[15] According to AARP findings there are ten class of drugs that cause cognitive impairment and they are Antianxiety drugs, Cholesterol drugs, Antiseizure drugs, Antidepressant drugs, Narcotic painkillers, Parkinson's



661

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Exercise in cancer and its benefits in cancer survivors

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Received: 14-11-2020 / Revised Accepted: 19-12-2020 / Published: 22-12-2020

ABSTRACT

This review focuses on the relationship between the cancer and physical activity along the continuum of cancer. Detecting a life-threatening disease like cancer and undergoing therapy can cause undesirable distress and interfere with standard of living. There is a wide array of epidemiological evidence to conclude that individuals involved in higher rates of physical activity are less likely to experience a number of cancers compared to those involved in lower levels of physical activity. Exercise enables survivors of cancer deal with and recovers from treatment; exercise can improve long-term cancer survivors' health and increase survival. Physical activity can be effective across the cancer spectrum. During cancer treatment the effects of physical activity are close to those felt after treatment. The results of this review support the belief that exercise is a relevant adjunct therapy in cancer treatment.

Keywords: Cancer, Exercise, Physical activity

INTRODUCTION

Worldwide, more than 10 million people are diagnosed with cancer, with advancement in early detection and management, it can be estimated that a growing number of patients will be alive five years after diagnosis. These people will join the rising number of cancer survivors, estimated at roughly 25 million.^[1] This realization has sparked a major research initiative into strategies for enhancing quality of life (QOL), reducing the likelihood of recurrence and other diseases, and expanding longevity in this population.^[2] Current cancer treatment, while increasingly effective in enhancing survival, is detrimental in many ways

and has harmful short- and long-term physiological and/or psychological effects, including pain, reduced cardiovascular capacity, cancer-related fatigue, reduced quality of life (QOL) and impaired immune function.^[3] There are two main types of health issues within the growing population of cancer survivors. The first concerns cancer recurrence and mortality. The second group encompasses the chronic adverse effects of treating cancer. Overweight, obesity and physical inactivity lead to the risk of developing a variety of cancers. Recognizing behavioural and environmental risk factors associated with cancer development, informing the public about these risk factors and offering strategies to modify exposure to these risk

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How to Cite this Article: Sharon Thomas, Mebin Alias, Venkateswaramurthy N. Exercise in cancer and its benefits in cancer survivors. World J Pharm Sci 2020; 9(1): 14-21.

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Exploring repurposed drugs in the treatment of various diseases

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Received: 19-10-2020 / Revised Accepted: 26-11-2020 / Published: 30-11-2020

ABSTRACT

Drug repurposing is a revolutionary method, as it offers new labels for already licensed and proven drugs. Drug repurposing has the potential to furnish new therapeutic alternatives for patients, deliver relevant clinical improvements while reducing the clinical development time of molecules in contrast to the de novo development of a new chemical entity, offering an economic merit by reducing the development times of medicines, but also by optimizing affordable medicines of high quality such as generic medicine. Owing to high cost and failure rates associated with conventional drug manufacturing methods, many pharmaceutical firms concentrate primarily on drug repurposing strategies. This review addresses the advantageous effects of the available approved medication compounds that can be used as repurposed medications for the treatment of other disease or condition such as cancer, respiratory diseases, tuberculosis, depression, Parkinsonism and schizophrenia.

Key Words: Drug repurposing, Cancer, Respiratory diseases, Tuberculosis, Neurological diseases.

INTRODUCTION

Drug repurposing is a term that has been entrenched for several years and relates to the use of the same pool of potentially re-positioned, re-formulated molecules, or coupled with new technical platforms and services^[1]. Drug repurposing has the ability to provide novel therapeutic substitutes for patients, to produce substantial clinical benefits while shortening the time of clinical development of drugs, as compared to the de novo development of a new chemical

entity, giving economic merit by reducing the time of development of medications, as well as by enhancing affordable high-quality medications such as generic medicine. The research circle increasingly recognizes the importance of drug repurposing, as seen in the public, non-profit and private sector efforts in this field. The added value of medicinal products represents an opportunity for society to resolve a range of medicinal inefficiencies in healthcare related to the excessive use of medicinal products, the lack of appropriate treatment choices, the scarcity of mature drugs,

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How to Cite this Article: Adithya K.L., R. Sambath Kumar, N. Venkateswaramurthy. Exploring repurposed drugs in the treatment of various diseases. World J Pharm Sci 2020; 8(12): 122-134.

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PRINCIPAL
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Gut microbita and probiotics in anti-cancer therapy: A promising future

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Received: 14-11-2020 / Revised Accepted: 12-12-2020 / Published: 22-12-2020

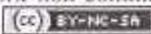
ABSTRACT

Cancer is a significant wellbeing trouble with multifactorial pathology, and is the second conspicuous reason for worldwide deaths. Regardless of all ongoing advancements in the clinical administrations, protection from standard medications and antagonistic impacts actually speak to a significant reason for treatment failure and helpful disappointment in cancer. Researchers are trying to look forward for inventive treatments and prophylaxis in cancer therapy. The statistics shows that cancer threats are indubitably influenced by immunological condition and genetic factors of the organism. There are growing evidences about the responses of chemo as well as immunotherapeutic medications by regulating the efficacy or toxicity by gut bacteria as well as preserving host's health and to maintain balanced homeostasis. A number of metabolites as well as bio products which are necessary to safeguard host's and gut's homeostasis are produced by Gut resident bacteria. Furthermore, intratumor bacteria can possibly regulate chemotherapy reaction. Microbiota compositions are specifically affected by anticancer therapy. Importantly, gut microbiota effectively relate with host by directly modulating the immune system or the gut epithelium. Several gut populating bacteria, named probiotics, were recognized as defensive against the growth of cancer cell. With their known ability to preserve gut homeostasis, probiotics are presently studied to battle dysbiosis in patients who are undergoing chemotherapy as well as radiotherapy. The profoundly critical examinations, revealing the tight connection among gut microbiota with tumorigenesis, along with gut microbiota, probiotics and anti-cancer treatment, are described in this review.

Keywords: Microbiota, Probiotics, Cancer, Anti-cancer therapy

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How to Cite this Article: Merin Shaji, Sambathkumar R and Venkateswaramurthy N. Gut microbita and probiotics in anti-cancer therapy: A promising future. World J Pharm Sci 2020; 9(1): 22-33.

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Melatonin as an add on therapy for SARS CoV-19 pandemic

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Received: 02-11-2020 / Revised Accepted: 30-11-2020 / Published: 02-12-2020

ABSTRACT

COVID-19 has been reported in over 4.1 million people worldwide as of May 11, 2020 and has resulted in more than 2,83,000 deaths. As of June 6, globally 66,63,304 confirmed cases and 3,92,802 deaths. More than 180 countries on all continents except Antarctica have reported laboratory-confirmed cases of COVID-19. Unlike SARS-CoV, however, which infected just 8,000 people worldwide in 8 months, the new SARS-CoV-2, estimated to be up to 1,000 times more infectious than SARS-CoV or other coronaviruses, has already infected more than 1,20,000 people worldwide in under three months. Melatonin (N-acetyl-5-methoxytryptamine) is a serotonin derivative bioactive molecule released from the pineal gland in the brain with an array of health-promoting properties. Melatonin slows and inhibits thymic involution, and promotes thymocyte regeneration and indirectly regulates the expression of ACE2, a key entry receptor involved in human coronavirus virus infection, like 2019-nCoV / SARS-CoV-2. Melatonin can act as a hormone, paracrine, autocrine or tissue factor to coordinate immune system function. Although melatonin has various properties in different cells of the body, it actively involved in reducing viral infections.

KEYWORDS: Melatonin, SARS-CoV, Viral diseases, Melatonin receptors

INTRODUCTION

Viral diseases continue to arise, and pose a significant public health problem, according to the World Health Organization (WHO).¹ Many viral epidemics, such as the Severe Acute Respiratory Coronavirus Syndrome (SARS-CoV) in 2003 affected more than 8,000 people worldwide with a mortality rate of 10%² and H1N1 influenza in 2009, have been reported in the last twenty years. Most

recently, Saudi Arabia first described Middle East Respiratory Coronavirus Syndrome (MERS-CoV) in 2012 which is closely related and caused by acute pneumonia similar to SARS-CoV.^{3,4} And in December 2019, a novel corona virus designated SARS-CoV 2 has caused an international outbreak of respiratory illness termed Novel Corona virus.² COVID-19 has been reported in over 4.1 million people worldwide as of May 11, 2020 and has resulted in more than 2,83,000 deaths. As of June

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How to Cite this Article: Dona Thomas, Sumitha S. K, Venkateswaramurthy N. Melatonin as an add on therapy for SARS CoV-19 pandemic. World J Pharm Sci 2020; 8(12): 152-161.

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KOMARAPALAYAM - 638 183.

ISSN 0975-4407 (Print)
2321-5836 (Online)
DOI: 10.5958/2321-5836.2020.00005.1

Vol. 12| Issue-01|
January- March, 2020

Available online at
www.anvpublication.org

**Research Journal of Pharmacology and
Pharmacodynamics**
Home page www.rjppd.org



REVIEW ARTICLE

Review on Antioxidant Supplements use in Cancer Chemotherapy

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ABSTRACT:

Reactive oxygen species (ROS) are by-products of metabolism that increase in the body during inflammation, smoking, radiation exposure and certain drugs. ROS damages DNA and other molecules and is involved in cancer growth and advancement. ROS can be neutralized and killed by the Endogenous and nutritional antioxidants and also play a part in the prevention of cancer. Human observational studies indicate that high intakes of foods rich in antioxidant, particularly fruits, vegetables, and grains, are inversely related to cancer risk. Radiotherapy and certain chemotherapeutic agents target on ROS to destroy cancer cells. Although supplementation with antioxidants may assist safeguard normal cells from ROS harm and may have palliative impacts during cancer treatment, studies shows that cancer cells can also be protected from ROS harm, thus reducing the efficacy of therapy and patient survival. This paper reviews shows the use of antioxidant supplements and antioxidant-rich diets in effect of cancer risk and mortality. A large number of patients undergoing cancer treatment uses antioxidants but antioxidants alone cannot be used as chemotherapeutic agent but it is proved to improve the therapeutic outcome and improvement in patient complaints when used as an adjuvant in chemotherapy. Antioxidants plays a major role in maintains of immune system but their actions in targeted area of cancer cells are idiopathic so, further studies have to be done independently in each antioxidant to establish its safety and efficacy.

KEYWORDS: Reactive oxygen species, Antioxidants, Cancer, Radiotherapy, Mortality.

INTRODUCTION:

Cancer is the primary cause for the death in united states of America.¹ The estimated rate of new Cancer cases in America was 16,688,780 and cancer death was 600,920 in the year of 2017. Death are prominent by their unlimited replicative, underexpression of tumor suppressor gene, metastasis, and escape of apoptosis. Based on the species of reactive oxygen and free radical manufacturing, cancer progression is affected. In observational studies, fruit and vegetable-rich nutritional substances have elevated antioxidants that can reduce the risk of cancer by destroying reactive oxygen species.¹⁻⁵ Later studies have shown that the effectiveness of plant-rich diet in cancer prevention is ambiguous. For the

Received on 20.01.2020 Modified on 10.02.2020
Accepted on 18.02.2020 ©A&V Publications All right reserved
Res. J. Pharmacology & Pharmacodynamics 2020; 12(1):21-24
DOI: 10.5958/2321-5836.2020.00005.1



REVIEW ON DRUGS USED FOR MANAGEMENT OF PRE-DIABETESAswin Baiju¹, N. Venkateswaramurthy^{2*} and R. Sambathkumar³^{1,2}Department of Pharmacy Practice JKKNattaraja College of Pharmacy, Kumarapalayam, Erode, Tamil Nadu.³Department of Pharmaceutics JKKNattaraja College of Pharmacy, Kumarapalayam, Erode, Tamil Nadu.Article Received on
18 October 2020,Revised on 08 Nov. 2020,
Accepted on 28 Nov. 2020

DOI: 10.20959/wjpr202015-19345

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Pre-diabetes is the condition, which is used to classify patients with irregularly elevated blood glucose, but not as much as high to support the diagnosis of diabetes mellitus, but can progress to type 2 diabetes mellitus by life style changes. Lifestyle modifications, clinical advances and pharmacotherapy interventions in benefits have been observed in pre-diabetic individuals have shown the benefits in transformation back to normoglycemia and to diminish the incidence of diabetes. Metformin is the mostly recommended primary pharmacotherapy with lifestyle changes, unless it is contraindicated or not. It enhances the action of insulin by declining the amount of hepatic glucose production in the liver and mostly reduces the incidence of

pre-diabetes.

KEYWORDS: Pre-diabetes, diabetes mellitus, metformin, lifestyle changes.**INTRODUCTION**

Diabetes mellitus (DM), one of the utmost serious challenges for health care organizations all round the world. Around one third of the elderly have DM, more than 60% of those patients with DM die due to serious vascular diseases and a greater percentage of the very old population develops other geriatric illnesses related to DM.^[1,2] In the elderly, DM is clinically diverse and its foremost high-risk state, pre-diabetes intermediate state of hyperglycemia, is increasing. Currently, 50% of US adults greater than 65 years have pre-diabetes and around 5-10% of them turn out to be diabetic every year.^[3,4] It is posing a serious life threat to entire population of the world irrespective of stages of industrialization and development. The

ISSN 0975-4407 (Print)
2321-5836 (Online)
DOI: 10.5958/2321-5836.2020.00029.4

Vol. 12| Issue-4|
October – December| 2020

Available online at
www.anvpublication.org

*Research Journal of Pharmacology and
Pharmacodynamics*
Home page www.rjppd.org



RESEARCH ARTICLE

Study on Analysing of Risk Factors and Prevalance of Urolithiasis in the Tertiary Hospitals of Erode, Tamil Nadu

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ABSTRACT:

Aim and Objective: Urinary stone occurrence is predicted as 3% in all individuals and it affect up to 12% of the population during their lifetime. Urinary stone forms with standard range of 50% at 10 years of age and male has the highest proportion. Due to various etiological and risk factors it became a great burden socially and economically. So it is relevant to conduct a study on risk factors and prevalence associated with urolithiasis.

Materials and Methods: A total of 110 patients were followed over a period of 9 months, and the prevalence and risk factors was studied. Data was collected with a self-administered questionnaire. **Results:** The prevalence of stones have markedly increased over the past 30 years and is of great concern in aging population. Out of 110 patients we found that 54.5% were females, 65% were in between the age 45-65 years, 39.9% stones are between 9-12mm, 39.09% of stone prevalence was at climate 84-86 °F, 72% were smokers, 35.45% were hypertensive patients, 55.45% had improper fluid intake and 21.8%. **Conclusion:** The relationship between the risk factors and prevalence had been established. The data shows the risk factors has a higher impact in formation of urolithiasis. The prevalence of urolithiasis was increased in higher temperature as a result of imbalance between input and output of fluids.

KEYWORDS: Urolithiasis, risk factors, prevalence.

INTRODUCTION:

The utmost preminent prevalent urological disorder of the urinary system is lithiasis.¹ Urolithiasis are minuscule hard crystal evolution from uric acid or calcium, magnesium, ammonium ion phosphate, calcium oxalate which is found to be hasten in urine, start to get built up in the inner surface of the kidney.² Risk factor and mortality rate of urolithiasis is increasing widely, although there is still significant rate of renal deterioration with certain stone types.

The geographic role of stone disease roughly tends to associate with environmental risk factors, a higher prevalence of stone disease is erect in hot arid, or dry climate such as mountain, desert or tropical area. The dietary factors will also influence the stone recurrence and formations.

The body weight and body mass index have a major impact in incidence of stone formation.³ With the changes in the socio economic conditions there will be a gradual change in the prevalence, incidence and distribution for age, sex, and type of urolithiasis in terms of both the site and the chemical-physical composition of calculi. The prevalence rate of the stone disease can be determined through a thorough understanding of risk factors, epidemiology and pathogenesis of urinary tract stone disease is necessary so as to develop an effective

Received on 07.11.2020 Modified on 18.11.2020
Accepted on 24.11.2020 ©AandV Publications All right reserved
Res. J. Pharmacology and Pharmacodynamics, 2020; 12(4):159-162.
DOI: 10.5958/2321-5836.2020.00029.4

