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Article Details

SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL EVALUATION OF NOVEL BIS-HETERO CYCLIC DERIVATIVES

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ABSTRACT

The present research outlines a series of bis-hetero cyclic derivatives (a1-6) synthesized from methyl-1-(2, 5-dioxopyrrolidin-1-yl) -6- methyl -2- oxo -4- phenyl -1, 2, 3, 4- tetrahydro pyrimidine -5- carboxylate treated with different aromatic aldehydes under acidic environment. The synthesized titled derivatives were confirmed by determination of physicochemical properties, by different spectral data and they were evaluated for in vitro antibacterial activity against Bacillus subtilis, Staphylococcus aureus, Escherichia coli and Pseudomonas aeruginosa and antifungal activity against Aspergillus niger and Candida albicans organisms at 25, 50, 100 µg mL-1 concentrations using streptomycin and fluconazole as reference standard drug respectively, through cup plate method. The in vitro antimicrobial assay results indicated that the derivatives a1, a2 and a3 showed significant antimicrobial activity, whereas the remaining derivatives showed moderate antimicrobial activities compared to the standard drugs. Further extension of this research to the cellular level is required to describe the mechanism of action, efficacy, and structural activity of these derivatives for antimicrobial activity.

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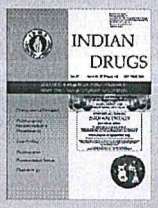

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ORIGINAL RESEARCH ARTICLES

SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL EVALUATION OF NOVEL BIS-HETERO CYCLIC DERIVATIVES

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ABSTRACT

The present research outlines a series of bis-hetero cyclic derivatives (a1-6) synthesized from methyl-1-(2, 5-dioxopyrrolidin-1-yl) -6- methyl -2- oxo -4- phenyl -1, 2, 3, 4- tetrahydro pyrimidine -5- carboxylate treated with different aromatic aldehydes under acidic environment. The synthesized titled derivatives were confirmed by determination of physicochemical properties, by different spectral data and they were evaluated for *in vitro* antibacterial activity against *Bacillus subtilis, Staphylococcus aureus, Escherichia coli* and *Pseudomonas aeruginosa* and antifungal activity against *Aspergillus niger* and *Candida albicans* organisms at 25, 50, 100 µg mL^{-1} concentrations using streptomycin and fluconazole as reference standard drug respectively, through cup plate method. The *in vitro* antimicrobial assay results indicated that the derivatives a1, a2 and a3 showed significant antimicrobial activity, whereas the remaining derivatives showed moderate antimicrobial activities compared to the standard drugs. Further extension of this research to the cellular level is required to describe the mechanism of action, efficacy, and structural activity of these derivatives for antimicrobial activity.

Keywords: Pyrrole, Pyrimidine, antibacterial, antifungal, cup plate method, Bis-Heterocyclic

INTRODUCTION

Bacteria and fungi are the frequent cause of organ dysfunction and infections, which can create life threats to humans[1]. Some of the microbes may become resistant to the existing drug due to their unnecessary usage and their infections may not be controlled with this drug[2]. Moreover, in current days, novel strains of microbial infections are coming to attack humans. Sometimes these microbial infections may or may not be controlled by the existing antimicrobial agents in the market[3]. So, there is an enormous scope for the development of novel antimicrobials to fight against novel and resistant microbial infections.

Heterocyclic chemistry is a special area of chemistry, which comprises the physicochemical, synthetic procedures, and various applications of heterocyclic compounds. Since the majority of the drug chemical structures are composed of heterocyclic compounds, it is known that these heterocyclic compounds are best and can be considered for drug development[4]. Compounds having two heterocycle rings fused with spacers are called bis-heterocyclic compounds. The utilization of bis-heterocycles has drastically increased in the field of medicinal chemistry for the design of biologically active compounds[5]. The bis-heterocyclic compounds containing nitrogen impart properties like biologically active, electronic, highly reactive, and wide range of solubility[6], these properties favor the medicinal chemist to select bis-heterocycles containing nitrogen like imidazole, pyrrole, pyrimidine, indole, triazoles, etc. scaffolds for design and development of novel biologically active compounds.

Pyrrole (Fig.1) is the most prominent scaffold among heterocyclic compounds and gains significant value in drug design and discovery. The pyrrole derivatives

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RESEARCH ARTICLE

Formulation and Statistical Evaluation of Tablets Containing Pitavastatin-Self Nano Emulsifying Drug Delivery Systems

Sridevi Gowripattapu[1,2], D. Sathis Kumar[1] and S. Selvamuthukumar[2,*]

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Abstract: ***Purpose:*** To formulate and characterize tablets containing Pitavastatin that have been loaded with a self-nano emulsifying drug delivery system (SNEDDS).

Methods: Pitavastatin SNEDDS were prepared with a variety of oils, surfactants, co-surfactants, and solvents to improve the dissolution rate and bioavailability of the HMG-CoA reductase inhibitor. The SNEDDS components were preliminarily investigated for drug solubility in various vehicles, excipient miscibility, emulsification rate, and ternary phase diagrams. The tablets were made using a porous carrier made of Aerosil 200 and then loaded with SNEDDS using a simple absorption method. Physical parameters such as tablet hardness, weight variation, disintegration, drug content, and *in-vitro* drug release were then measured on the tablets.

Results: Labrafac Lipophilew1349 (Oil), Tween 80 (Surfactant) and Egg lecithin (Co-surfactant) were selected for the preparation of SNEDDS. Tablets with high porosity suitable for loading with SNEDDS and containing the super-disintegrants, achieved complete dissolution of Pitavastatin from the tablets. In vitro release of Pitavastatin from SNEDDS and the tablets was similar ($p < 0.05$).

Conclusion: SNEDDS of Pitavastatin is a promising approach to achieving a solid dosage form of the liquid-loaded drug delivery systems for enhancing the solubility and dissolution rate of the drug, and hence also its bioavailability.

Keywords: Pitavastatin, drug carrier, SNEDDS, self-nanoemulsifying, solubility, drug release, surfactant, co-surfactant.

1. INTRODUCTION

Oral administration is the favourable method of noninvasive delivery since it is the easiest and most convenient. Drug molecules with low water solubility, on the other hand, face various challenges. Poor solubility in water affects about 40% of new compounds, which is a real problem for the novel drug delivery system just because it leads to a reduction in oral bioavailability, large intra- and inter-subject variability, and dosage proportionality. Class II drugs are those that fall within this category [1]. To tackle the poor aqueous solubility of drugs, enormous studies such as solid dispersion and complexation with cyclodextrins have already been used [2-7].

To be sure, in some selected cases, these methodologies were effective, yet unfortunately, in specific cases they lead to a negative impact, in solid dispersion, the measure of transporters utilized is frequently enormous and, accordingly, assuming the portion of the dynamic fixing is high, the tablets or containers framed will be huge in volume and hard to swallow. Moreover, the high production cost is due to the usage of freeze or spray-drying apparatus and also the carriers used in the product development. It would be difficult to handle co-precipitates, because of the high viscosity. Hence, in its place, the usual solvent approach might be used. Drug compounds that are not soluble in both aqueous and organic solvents cannot be complexed with cyclodextrin methods.

Lipid formulation gains great attention for improving the bioavailability of the poorly water-soluble drug, since it is hydrophobic, or more lipophilic. Nano-emulsion formed by low energy *i.e.* self-nano formation during dilution with the medium is an attractive manner because of its cost-friendly and simple technology method. Supersaturable self-nano emulsifying drug delivery system (S-SNEDDS) is a preconcentrate of lipid formulation comprising of oil, surfactant, and co-surfactant in which the drug is incorporated into them until the saturated condition is achieved at a predetermined condition. This formulation formed nanodroplet by dilution with medium. The S-SNEDDS formulation has several advantages which include the enhancement of drug effective-

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Design and Statistical Optimization of Pluronic Based Ibuprofen Gels by Box-Behnken Design and Their Physicochemical Characterization

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Aims and scope →

Harani Avasarala ✉, D. Sathis Kumar, Srijit Tripathy, Sathi Sravani, Veera Vimala devi & Shaike Kamaluddin

The present work was focused on the development of pluronic based ibuprofen gels for the purpose of increasing drug solubility with the aid of pluronic F127, pluronic L64, and propylene glycol additives as gelling agents and central composite design (CCD) expert software for optimizing their percentage content. The desired gels were formulated and evaluated for the gelation temperature and drug content as analyzed by the CCD expert software. Finally optimized gel formulations (OFs) were subjected to *in vitro* diffusion studies in terms of a kinetic fitting model. It was found that OF1 had the optimum concentrations in making effective pluronic based ibuprofen gels with desired response characteristics. Pluronic gels can be used as efficient means of formulation to enhance drug solubility and permeability which is confirmed by the results of *in vitro* diffusion studies and flux calculations.

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Review article

Engineered upconversion nanocarriers for synergistic breast cancer imaging and therapy: Current state of art

Pavan Kumar Chintamaneni [a], Dasari Nagasen [b,c], Katta Chanti Babu [d], Atul Mourya [d], Jitender Madan [d], Dadi A. Srinivasarao [d], R.K. Ramachandra [e,f], P. Madhuri Santhoshi [e], Sai Kiran S.S. Pindiprolu [b,c,*]

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ABSTRACT

Breast cancer is the most common type of cancer in women and is the second leading cause of cancer-related deaths worldwide. Early diagnosis and effective therapeutic interventions are critical determinants that can improve survival and quality of life in breast cancer patients. Nanotheranostics are emerging interventions that offer the dual benefit of in vivo diagnosis and therapeutics through a single nano-sized carrier. Rare earth metal-doped upconversion nanoparticles (UCNPs) with their ability to convert near-infrared light to visible light or UV light in vivo settings have gained special attraction due to their unique luminescence and tumor-targeting properties. In this review, we have discussed applications of UCNPs in drug and gene delivery, photothermal therapy (PTT), photodynamic therapy (PDT) and tumor targeting in breast cancer. Further, present challenges and future opportunities for UCNPs in breast cancer treatment have also been mentioned.

1. Introduction

Breast cancer is the major cause of cancer deaths in women (11.7% of total cases). According to the World Health Organization (WHO) report, 17.5 million breast cancer-related deaths can be expected per year, by 2050 [1]. Resistance to conventional therapies, metastasis and relapse of tumors are emerging as major causes of breast cancer-related deaths [2]. The currently available treatment approaches are limited due to their off-target effects on healthy tissues. Further, the majority of chemotherapeutic agents show limited bioavailability and tumor localization, due to their intrinsic properties. Hence, several drug delivery systems are being investigated to achieve site-specific (tumor site) accumulation of the therapeutic agent.

In the past few years, phototherapy is being extensively explored as an alternative to conventional chemotherapy. Depending upon the mechanism of anticancer activity, phototherapy can be further classified as photothermal therapy (PTT) and photodynamic therapy (PDT) [3]. PDT and PTT utilize light energy to generate reactive oxygen species (ROS) and heat respectively for selective photochemical and/or photothermal destruction of cancer cells [4]. However, they encounter a few drawbacks such as low tumor targetability, absence of bio-responsive character, short systemic half-life and reduced in-vivo ROS generation, etc. Apart from this, synthetic chemical sensitizing agents displays photo instability, high autofluorescence, broad emission peak and short fluorescence lifetime. The application of conventional molecular imaging agents for the detection of tumors like Bromine (Br), gadolinium (Gd), lead (Pb), uranium (U), Dysprosium (Dy), copper (Cu), Ytterbium (Yb), gold (Au), Bismuth (Bi), Lutetium (Lu) and organic dyes is limited due to their sensitivity, low cellular uptake and off-target toxicities. In recent years various nanocarriers are being widely studied for their application in the targeted delivery of imaging agents specifically to cancer cells [5].

In recent years, nanosized (up to 1000 nm) therapeutic carriers have been proven promising to overcome the limitations of conventional anticancer agents [6]. Delivery of anticancer agents via nanocarriers

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Article

Ethosomal gel: a novel choice for topical delivery of the antipsychotic drug Ziprasidone Hydrochloride

Harani Avasarala[1,2,3*], SathisKumar Dinakaran[1,3], Bhavani Boddeda[2], Sai Prasanna Dasari[2], Vijaya Ratna Jayanthi[2], Percy Swaroopa[2]

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Oral delivery of antipsychotic drugs like Ziprasidone HCl has a disadvantage of gastric disturbance and lack of adherence to the treatment. In the present study, Ziprasidone HCl loaded ethosomal gel was formulated to avoid the disadvantages of oral delivery.

The ethosomes were prepared using Lipoid S 75 with Isopropyl alcohol and Propylene glycol as the solvents. The formulated ethosomes were evaluated for different parameters like particle size, poly dispersibility index and entrapment efficiency. Based on diffusion studies, optimized ethosomal formulation was incorporated in carbopol 934 gel base. The final dosage form of ethosomal gel was evaluated for physical characteristics, drug content and proceeded with *ex-vivo* skin permeation studies.

The maximum percentage of drug permeated after 24 hours was found to be 93.30±0.168. The flux was found to be 52.05± 0.564µg/hr/cm^2. From the kinetic model fitting results, it was concluded that the ethosomal gel followed the first order kinetics and the higher "R^2" values of the Korsmeyer Peppas model (R^2=0.934, n=0.54) indicate that the encapsulating polymer is the responsible factor in controlling the release of the drug.

The ethosomal gel loaded with ziprasidone HCl improves the bioavailability of ziprasidone HCl as well as surpassing drawbacks with oral delivery.

Keywords: Ethosomes. Ziprasidone HCl,. Ethosomal Ggel. Lipoid S75,. Carbopol 934.

1. INTRODUCTION

Ethosomes, the lipid vesicular carrier systems, also called as alcoholic liposomes are composed of phospholipids, alcohol (ethanol and isopropyl alcohol) in relatively high concentration and water. Ethosomes are suitable carrier systems for both hydrophilic and lipophilic drugs. The small particle size of ethosomes (microns to nanometer) facilitates their potentiality in carrying the drug through the skin into systemic circulation. The ease of preparation, non- irritant nature, efficiency to encapsulate wide range of drug molecules and higher stability than any other vesicular systems makes the ethosomes the most opted carriers for topical delivery of drugs (Gangwar, Singh, Garg, 2010; Tarun *et al.*, 2013; Leon, Herbert, Joseph, 2009).

Although, the actual phenomenon by which the ethosomes enhance permeability is not clear, it is believed to enhance by various pathways. They involved disruption of stratum corneum (Dinesh *et al.*, 2010) or by getting themselves trapped in the follicles (i.e., pilosebaceous pathway). Ethosomes contains phospholipids entrapping alcoholic drug solutions. The phospho-lipids may vary from 0.5 to 10% in the formulations. The alcohols which can be a softener, vehicle and penetration enhancer along with glycol, constitute 22-70% of ethosomal formulations (Mamta, Anar, Rahul, 2013; Vaibhav, Dinesh, Jain, 2007; Manish, Lifeng, Sui, 2011). Through various studies, it was reported that varying the compositions of alcohol and water, the drug delivery can be modulated and thus the

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PATIENT-CONTROLLED SEDATION METHODS IN PHARMACOLOGY AND MEDICAL RESEARCH

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Abstract

Patient controlled sedation is nothing is a painless procedure, which is given to the patient. Many patients are opting for the general anesthesia procedure as it lead them with the painless affect during the surgery. It has been seen that most of people they have fear in the ways of giving sedation to the patients. It has also been observed that unprofessional doctors are using during levels methods and techniques for providing the sedation, which is neither accurate for the patient nor good for their careers too. Operation or the surgery cannot be done without giving anesthesia or the sedation. It is a process of pacifying the patient before any process. It can be in the form of medicines or the injections. These drugs help the patients in realizing the pain and eagerness before the surgery.

Keywords: General anesthesia, sedation, painless, relief, pharmacology, patient

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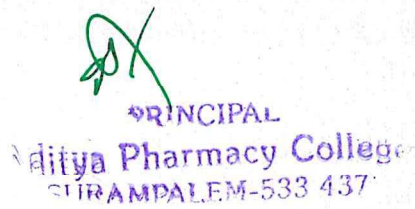

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Research Article

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FORMULATION AND *IN-VITRO* EVALUATION OF VERAPAMIL HCl FAST DISINTEGRATING TABLETS USING *OCIMUM GRATISSIMUM* SEED MUCILAGE POWDER AND *CUCURBITA MAXIMA* PULP POWDER

Chirravuri. S. Phani Kumar[1*], Gummadi Ramakrishna[1], Gurajapu Sai Sandhya[2], B. Chandra Sekhar[2], Kuppili Anusha[2] and D. Deepika[2]

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ABSTRACT

Verapamil HCl belongs to the BCS class 2 drug, hence its oral bioavailability is poor. Bioavailability is very important for every drug to get good biological activity. Dissolution is directly proportional to the bioavailability and disintegration is directly proportional to the dissolution. Hence, in this current study *in-vitro* dissolution was increased with the help of increasing disintegration. Fast disintegrating tablets of verapamil HCl were designed with the help of *Ocimum gratissimum* seed mucilage powder and *Cucurbita maxima* pulp powder as natural super disintegrants at 2.5, 5 & 10% w/w per tablet and compared with croscarmellose sodium, a synthetic super disintegrant. And found that *Ocimum gratissimum* seed mucilage powder had best *in-vitro* disintegration and dissolution characteristics compared to other two super disintegrants and at 10% w/w per tablet i.e., F10 formulation had shown best *in-vitro* dissolution compared to croscarmellose sodium and was considered as final formulation.

Keywords: Fast disintegrating tablets, natural disintegrants and synthetic super disintegrant.

INTRODUCTION

Newly discovered drugs are tried to formulate as tablets, because of possibility of self-administration and doesn't require any technician. And tablets are the best formulations among the solid oral dosage forms with respect to the dose accuracy. They are pilfering proof dosage forms; the incorporated dose to the tablet dosage form is completely available to the systemic circulation if drug doesn't suffer from solubility. If drug suffers from the solubility, then it suffers from oral bioavailability. The drug bioavailability may be increased by enhancing solubility by various methods like decreasing crystallinity, converting crystalline drug to amorphous solid, by increasing disintegration and by increasing dissolution. Enhancement of disintegration is one of the mostly used method for enhancing drug bioavailability by enhancing drug dissolution. This technique is used widely for the greatest number of drugs that are suffered from poor solubility[1].

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Method development and validation for the simultaneous estimation of amlodipine besylate and atorvastatin calcium in pharmaceutical dosage forms by micellar liquid chromatography

Pulagurtha Bhaskararao, Kontham Venkataramanapa Raju and Balla Sujiya

Abstract
The present study is aimed at developing and validating an accurate, precise, linear and robust micellar liquid chromatographic method for the simultaneous estimation of amlodipine besylate (AB) and atorvastatin calcium (AC) in pharmaceutical dosage forms. The analysis of AB and AC is done with a mixture of *n*-butanol and polysorbate 20 (0.05 M) in the ratio of 30:70 (v/v) as mobile phase and Phenomenex C18 column (150 mm × 4.6 mm, 5 µm) as stationary phase. The chromatographic peaks of AB and AC were detected and measured at 240 nm. The retention times of AB and AC were found to be 3.61 min and 6.53 min, respectively. The developed method is demonstrated to access its suitability for meeting its intended purpose by the validation with a set of validation parameters as per ICH and USP guidelines. The method is proved to be linear from 5 to 50 µg/ml for AB and 10 to 100 µg/ml for AC with the correlation coefficients of 0.9995 and 0.9990, respectively. The method is found to be precise with percent relative standard deviation value in range 0.8-1.1% and 0.5-1.0% and accurate with recoveries of 99.20 to 101.20% and 98.80 to 100.67% for AB and AC respectively.

Keywords: Amlodipine besylate, atorvastatin calcium, polysorbate 20, micellar liquid chromatography, stability indicating, analysis

Introduction
Amlodipine besylate (AB), chemically called as (3-ethyl 5-methyl 2-[(2aminoethoxy o methyl]-4-(2chlorophenyl)-methyl 1,4 dihydropyridine,3,5dihydrocarboxylate), is a dihydropyridine and long-acting potent calcium channel blocker used for the treatment of hypertension, congestive heart failure and angina pectoris[1]. AB lowers the blood pressure, relaxes the heart muscles and dilates the heart blood vessels to prevent spasm [2, 3]. Chemical structure of AB is given in Fig 1. Atorvastatin calcium (AC), described chemically as ([R-(R*, R*)]-2-(4-fluorophenyl)-β, δ-dihydroxy-5-(1-methylethyl)-3-phenyl-4-[(phenylamino) carbonyl] -1H-pyrrole-1-heptanoic acid, calcium salt (2:1) trihydrate). AC is an antihyperlipidemic agent belonging to drug class statins [3]. AC is widely used in the treatment of hypercholesterolemia. AC decreases the levels of low-density lipoproteins and triglycerides to a major extent and slightly increases the level of high-density lipoprotein [4]. Chemical structure of AC is given in Fig 1.

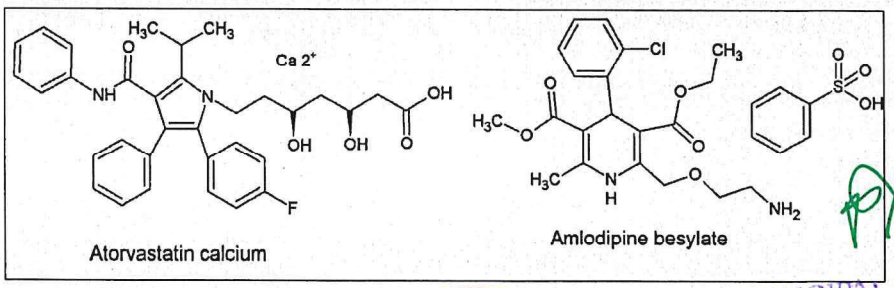

Fig 1: Structure of amlodipine besylate and atorvastatin calcium

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TO WHOMSOEVER IT MAY CONCERN

This is to certify that, number of books and chapters in edited volumes/books published and papers published in national/ international conference proceedings per teacher during last five years are 1, details were given below

S. No.	Academic Year	No. of Books/Chapters	Details
1.	2022-2023	1	

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ADVANCEMENT OF THE FEMALE REPRODUCTIVE PHASES CORRELATED WITH POSTMENOPAUSAL COMPLICATIONS INTENSIFICATION: CURRENT APPROACHES TO THE PREVENTION AND TREATMENT

Abstract

Women go through menopause naturally as they age. Many women transition into menopause with few or no symptoms, while others experience severe or even incapacitating symptoms. When female gynaecologist Trotula of Salerno stated that "there are older women who put forth blood matter especially when menopause approaches them" in the 11th century, we had a very different notion of the menopause. However, little is understood regarding the effects of menopause on women's mental health, particularly in the case of severe and persistent conditions like schizophrenia. Many postmenopausal women get vulvovaginal atrophy, which is brought on by an inadequate oestrogen supply. Vaginal dryness, itching, irritation, and dyspareunia are symptoms. Oestrogen therapy was the usual for lowering bone loss when a link between menopause and osteoporosis was first recognised in the past, but there was little information on fracture prevention even though it was thought to be effective. Up until the Women's Health Initiative (WHI) research published data on 6 years of hormone therapy treatment in 2001, which showed an increase in heart attacks and breast cancer, this persisted. Patients were concerned and there was a significant decline in oestrogen use even though the hazards were minimal (1 per 1500 users annually). In further analyses, the WHI trial demonstrated that oestrogen in women between the ages of 50 and 60 really decreased fractures and averted heart attacks.

Keywords: Vulvovaginal atrophy, WHI, Dyspareunia, Vaginal dryness

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