Farmaceutska komora
Crne Gore
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FARMACEUTSKI FAKULTET

CALIMS

U SARADNJI SA AGENCIJOM ZA LJEKOVE I MEDICINSKA SREDSTVA CRNE GORE

II KONGRES FARMACEUTA CRNE GORE SA MEĐUNARODNIM UČEŠĆEM
II CONGRESS OF PHARMACISTS OF MONTENEGRO WITH THE INTERNATIONAL PARTICIPATION

ZBORNIK SAŽETAKA
ABSTRACT BOOK

FARMACIJA – NAUKA I PRAKSA VOĐENE HUMANOŠĆU
PHARMACY - SCIENCE AND PRACTICE GUIDED BY HUMANITY

28-31.MAJ 2015. BUDVA, HOTEL SPLENDID

POD POKROVITELJSTVOM

MINISTARSTVO ZDRAVLJA
CRNE GORE

fip

glosarij

II Kongres farmaceuta Crne Gore sa međunarodnim učešćem
Zbornik sažetaka

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Tiraž: 650
Dizajn: PRiSMA – korporativne komunikacije
Štampa: Foto Nikić Digital
Rukopisi se ne vraćaju

BODY DETOXIFICATION OF HARMFUL SUBSTANCES IN THE ENVIRONMENT

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Our body is burdened not only with process of digestion of poor and unhealthy food, but also with elimination of pesticides, contamination and toxic substances which get into our body through the environment and food. In addition to this, there are stress, too fast way of living and lack of physical activities which also burden and weaken our body and disturb its regular functioning. Irregular body functioning may provoke some smaller issues such as tiredness and sleepiness, but further on it may cause bigger problems like depression, premature aging and many other conditions. We cannot avoid toxins because they are all around us. Toxins and heavy metals pollute water, air and food. On a daily basis, we use cosmetic as well as products for personal hygiene which are full of dangerous chemicals. Once they enter our body, heavy metals are being accumulated in internal organs, tissues and bones. The body itself cannot eliminate them without our help. Available detoxification tools, besides physical ones (clay, zeolite, cold-pressed and essential oils) include: silence, nature sounds, relax music.
To emphasize the importance of timely acting regarding the body cleaning of toxic substances, in order to recover the energy and improve overall health.
Based on study of available books, publications of domestic experts for detoxification, people's experience as well as on our own experience.
Showed that the detoxification or body cleaning effect helped people regain their natural body balance. Many people assert they managed to recover energy, concentration and positive state of mind.
There are many ways of body detoxifications. Although almost every wellness center offers the detoxification treatment, there should be no rush, because nature bestows simple and free ways of body cleaning on us.

Keywords: Detoxification, toxins, symptoms, detoxification products, detoxifications treatments.

3D-QSAR STUDIJA I RAZVOJ FARMAKOFORE ZA DIZAJN NOVIH ANTIDEPRESIVA SA DEJSTVOM NA TRANSPORTERE SEROTONINA I HISTAMINSKE H3 RECEPTORE

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Depresija je najčešći mentalni poremećaj koji pogađa oko 350 miliona ljudi širom sveta. Selektivni inhibitori preuzimanja serotonina (SSRIs- Selective Serotonine Reuptake Inhibitors) su lekovi izbora u lečenju depresije. Rezidualni simptomi (umor, kognitivna disfunkcija, poremećaji spavanja itd.) predstavljaju značajan problem u terapiji ovog poremećaja. Antagonisti H3 receptora poboljšavaju kognitivnu funkciju i povećavaju budnost, bez nespecifičnog stimulatornog efekta, što otvara mogućnost njihovog kombinovanja sa SSRIs u cilju prevazilaženja problema rezidualnih simptoma. Do danas su sintetisana mnoga jedinjenja sa dvostrukom aktivnošću inhibitora preuzimanja serotonina/antagonista H3 receptora.

Cilj rada je bio formiranje 3D-QSAR modela i strukture farmakofore jedinjenja sa dualnom aktivnošću inhibitora preuzimanja serotonina i antagonista histaminskih H3 receptora i dizajn novih antidepresiva koji ostvaruju efekat na oba ciljna mesta.
Iz literature su preuzeti podaci o strukturi i aktivnosti dualnih inhibitora preuzimanja serotonina/antagonista H3 receptora. Za pripremu molekula su korišćeni Marvin Sketch program, komponente ChemOffice paketa i Gaussian 98W. 3D-QSAR (3D Quantitative Structure-Activity Relationship) studija je sprovedena pomoću programa Pentacle 1.0.6.
Formiran je 3D-QSAR model SERT (Serotonin Reuptake Transporter) inhibitora i 3D-QSAR model antagonista H3R i konstruisane su 3D-strukture farmakofora za oba ciljna mesta. Definisane su strukturne karakteristike ispitivanih jedinjenja sa najvećim uticajem na aktivnost na SERT i H3R. Oba 3D-QSAR modela su ukazala na odgovarajućeg donora vodonične veze i supstituisanu fenil grupu sa optimalnim sternim i hidrofobnim osobinama kao značajne grupe za aktivnost na oba ciljna mesta. Stoga, uvođenjem odgovarajućeg supstituenta u fenil grupu, dizajnirani su novi ligandi. Dizajnirani ligandi sa predviđenom pKi(SERT)>8,42 i sa predviđenom pKi(H3R)>8,39 odabranu su za dalju studiju.
Formirane 3D-strukture farmakofora su upotrebljene za dizajn novih dualnih SERT/H3R inhibitora. Prednost dizajniranih jedinjenja u odnosu na polazna ogleda se u većoj aktivnosti na H3R uz zadržavanje optimalne aktivnosti inhibitora preuzimanja serotonina.

Ključne reči: Dizajn lekova, antidepresivi, 3D-QSAR, SSRI, antagonisti H3 receptora

3D-QSAR STUDY AND PHARMACOPHORE DEVELOPMENT OF NOVEL ANTIDEPRESSANTS AFFECTING SEROTONINE TRANSPORTERS AND HISTAMINE H3 RECEPTORS

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Depression is the most prevalent psychiatric disease, affecting 350 million people worldwide. Selective serotonin reuptake inhibitors (SSRIs) are the most frequently prescribed antidepressant drugs. Residual symptoms (fatigue, cognitive dysfunction, sleep disturbance etc.) are important problem in therapy of depression. Since H3 receptor (H3R) antagonists improve cognition and increase wakefulness without showing nonspecific stimulant effects, development of novel dual acting antidepressants affecting serotonin transporters and histamine H3 receptors is potential solution to residual symptoms problem. To the present, many compounds with dual activity have been synthesized.
The aim of this study was to create 3D-QSAR models and pharmacophore structure of dual serotonin transporter/histamine H3 ligands and to design novel ligands as potential antidepressants.
Information about structure and activity of dual serotonin transporter/histamine H3 ligands was taken from references. Molecules were prepared in Marvin Sketch, ChemOffice and Gaussian 98W programs. 3D-QSAR (3D Quantitative Structure-Activity Relationship) analysis was performed by Pentacle 1.0.6 program.
Two 3D-QSAR models have been built, SERT (Serotonin Reuptake Transporter) model and H3R model, and 3D-pharmacophore structures have been constructed. Structural features

important for activity on both target sites have been defined. The 3D-QSAR models revealed specific hydrogen bound donor and substituted phenyl group with optimal steric and hydrophobic features as the structures significant for activity on both target sites. Therefore, by introducing the appropriate substituent into phenyl group, novel ligands have been designed. Designed ligands with predicted pKi(SERT)>8,42, and predicted pKi(H3R)>8,39 were selected for further evaluation.
Formed 3D-pharmacophore structures have been used for design of novel dual serotonin transporter/histamine H3 ligands. Advantage of designed ligands compared with the lead, is that designed ligands have higher activity on histamine H3 receptor, while they maintain optimal activity on SERT.

Key words: Drug design, Antidepressants, 3D-QSAR, SSRI, H3 receptor antagonist

PARENTERALNE NANOEMULZIJE DIAZEPAMA SA 20, 30 I 40% ULJANE FAZE: FIZIČKOHEMIJSKA I BIOFARMACEUTSKA KARAKTERIZACIJA

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Poznato je da parametri formulacije, kao i parametri procesa izrade, mogu značajno da utiču na fizičkohemijska svojstva i stabilnost nanoemulzija. Pored toga, od velikog značaja je i razumevanje uticaja same formulacije na ponašanje inkorporiranog leka – oslobađanje iz nanoemulzija, farmakokinetičko ponašanje i, posledično, terapijski efekat. Cilj ovog rada bio je da se razviju parenteralne nanoemulzije sa diazepamom kao model lekovitom supstancom i da se sprovede njihova sveobuhvatna fizičkohemijska i biofarmaceutska karakterizacija.
Metodom homogenizacije pod visokim pritiskom izrađene su nanoemulzije diazepama, stabilizovane smešom lecitina i polisorbata 80, variranjem udela uljane faze – 20, 30 i 40% (m/m) smeše triglicerida srednje dužine lanca i sojinog ulja u odnosu 4:1. U istraživanju je praćen uticaj koncentracije uljane faze na veličinu kapi (Z-Ave), indeks polidisperznosti (PdI), zeta potencijal (ZP) i fizičku stabilnost nanoemulzija. Takođe, praćen je uticaj broja ciklusa homogenizacije na Z-Ave i PdI u cilju identifikovanja optimalnih uslova za izradu nanoemulzija. Primenom reverzne tehnike sa dijaliznim vrećicama sprovedeno je in vitro ispitivanje brzine oslobađanja diazepama iz razvijenih nanoemulzija, uz karakterizaciju dobijenih profila oslobađanja primenom različitih matematičkih modela.
Nakon izrade, sve formulacije imale su prosečnu veličinu kapi u opsegu 197–211 nm, sa veoma uskom distribucijom veličine (PdI: 0,102–0,124), dok je ZP bio oko –50 mV. Tokom 2 meseca čuvanja na 25°C, sve nanoemulzije bile su fizički stabilne, bez značajnih promena u praćenim parametrima. In vitro ispitivanje brzine oslobađanja pokazalo je da su profili oslobađanja diazepama iz ispitivanih nanoemulzija sa 20, 30 i 40% uljane faze slični i da se 40–50% diazepama oslobodi iz ovih nanoemulzija u toku 1 h, pri čemu se kinetika oslobađanja može opisati Korsmeyer-Peppas modelom.