LEMBAR
HASIL PENILAIAN SEJAWAT SEBIDANG ATAU *PEER REVIEW*
KARYA ILMIAH : JURNAL ILMIAH

Judul Karya Ilmiah (Artikel) : Difference of Tumor Necrosis Factor (TNF-α) Levels in Multibacillary Leprosy between Reversal Reaction and Non-reversal Reaction Patients
Jumlah Penulis : 4 Orang
Status Pengusul : **Renni Yuniati**, Fatihatul Firdaus Munita, BAZILAH Dayana, FIKA Amalia
Identitas Jurnal Ilmiah :
a. Nama Jurnal : Pak J Med Health Sci
b. Nomor ISSN : 19967195
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d. Edisi : Jul –Sept 2018
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f. Jumlah halaman : 3
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h. Alamat web jurnal : https://pjmhsonline.com/2018/july_sep/pdf/1381.pdf
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j. On line turnitin :
https://doc-pak.undip.ac.id/9138/1/Turnitin_Difference_of_Tumor_Necrosis_Factor.pdf

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c. Kecukupan dan kemutahiran data/informasi dan metodologi: studi analitik observasional dengan desain belah lintang, data diperoleh dengan pemeriksaan imunohistokimia yg terstandar, tersaji dengan gambar dan tabel
d. Kelengkapan unsur dan kualitas terbitan/ jurnal: Pak J Med Health Sci, penerbit: Department Of Surgery, Mayo Hospital, merupakan Jurnal Ilmiah Internasional bereputasi, terindeks scopus Q4, SJR 0,114

Semarang, 10 Desember 2021
Reviewer 1

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b. Ruang lingkup dan kedalaman pembahasan : Penelitian ini bertujuan untuk mengetahui perbedaan kadar TNF-α pada both multibacillary leprosy patients with and without reversal reaction. Penelitian sangat sesuai dengan bidang ilmu. Pembahasan mendalam dengan mensitasi 16 pustaka dimana >80% pustaka primer.
c. Kecukupan dan kemutahiran data/informasi dan metodologi: Penelitian cross sectional yang dibagi menjadi dua kelompok masing-masing terdiri dari 28 pasien kusta tanpa reaksi balik. Kadar TNF-α diukur dengan pewarnaan imunohistokimia. Tingkat TNF-α pada kedua kelompok masing-masing dianalisis menggunakan independent sampel uji T.
d. Kelengkapan unsur dan kualitas terbitan/ jurnal: Terbitan lengkap memuat vol, no, tahun dan daftar isi dan terindeks di SCOPUS, namun tidak ada DOI

Semarang,
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PAKISTAN JOURNAL OF MEDICAL & HEALTH SCIENCES

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Original article: maximum 3000 words excluding title page and a structured abstract of 250 words and references with no more than three tables or figures and 25 references Short Reports / Short Communications / Special Communications / Case reports: maximum 1250 words excluding title page and an unstructured abstract of 150 words and references with no more than two tables or figures and 10 references. It should not be signed by more than six authors.

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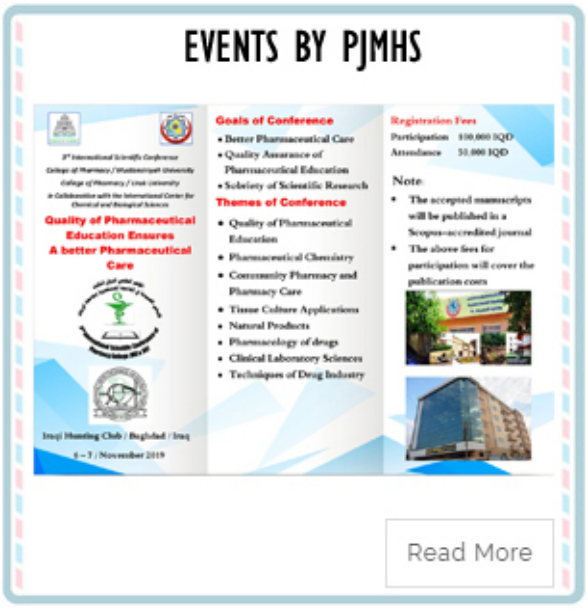

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ORIGINAL ARTICLE

3D QSAR Studies of 2-Arylpyrimidines and S-Triazines as Selective PDE4B Inhibitors

ANAND GAURAV, DHARMENDRA KUMAR

ABSTRACT

Background: Phosphodiesterase 4B (PDE4B) has emerged as important target for design of anti-inflammatory drugs for respiratory tract. Several selective PDE4B inhibitors are under various stages of development, among them 2-arylpyrimidines and s-triazines have been identified as inhibitors with high degree of selectivity for PDE4B. However, the structural features responsible for the PDE4B selectivity of these molecules have not been identified and explored so far.

Method: 3D QSAR studies were performed for the series of 2-arylpyrimidines and s-triazines using Accelrys Discovery Studio 3.5. The IC_{50} values were transformed to PDE4B selectivity by taking the ratio of IC_{50} values i.e. PDE4D(IC_{50})/PDE4B(IC_{50}) for all the molecules in the series, and used as the dependent variable. The dataset was divided into training and test set of 45 and 10 compounds respectively and 3D QSAR was performed using the default parameters. Test set prediction and Fischer statistic was used for validation of the developed model.

Results: Statistically robust and predictive 3D QSAR models with high r^2_{cv} value of 0.9794 were obtained. The contour maps revealed the sterically and electronically favourable and unfavourable regions around the 2-arylpyrimidines and s-triazines scaffolds.

Conclusion: 3D QSAR model for 2-arylpyrimidines and s-triazines as selective PDE4B inhibitors were developed and validated. The models were highly predictive and provided vital structural information for the design of newer and more selective PDE4B inhibitors having the 2-arylpyrimidine and s-triazines scaffold. The results of the present study will be followed up by the design, synthesis and experimental evaluation of newer selective PDE4B inhibitors.

Keywords: Cyclic Nucleotide Phosphodiesterases, Type 4B; 3D Quantitative Structure-Activity Relationship; Fischer statistic; 2-arylpyrimidines; s-triazines

INTRODUCTION

Prevalence of Inflammatory diseases of respiratory tract i.e., asthma and COPD has increased in recent years, with more than 200 million people affected by it worldwide. Most of the mortality related to these inflammatory disorders occurs in low- and low middle income countries[1].

Phosphodiesterase 4 (PDE4) is a major family of enzymes that selectively hydrolyze 3',5'-cyclic adenosine monophosphate (cAMP) and are involved in regulating the release of anti-inflammatory and pro-inflammatory cytokines within cells[2,3,4]. Even though PDE4s are widely expressed in immune and inflammatory cells, levels of different PDE4 subtypes (PDE4A, PDE4B, PDE4C and PDE4D) vary in a specific cell. PDE4B is abundant in monotypes and neutrophils, while PDE4A is expressed to very low levels and PDE4C is absent in inflammatory cells[5,6,7,8,9]. This makes PDE4B an interesting and promising targets for anti-inflammatory drugs meant to be used in respiratory inflammatory diseases such as asthma and chronic obstructive pulmonary disease (COPD). Inhibition of PDE4 has been shown to suppress a diverse spectrum of inflammatory responses *invitro* and *in vivo.*[10-13] More importantly, many PDE4 inhibitors in development are efficacious in animal models of various inflammatory disorders, such as asthma, COPD, psoriasis, inflammatory bowel diseases, and rheumatoid arthritis[11,14,15], as well as in clinical trials for asthma and COPD[16,17,18]. However the development of PDE4 inhibitors has been slowed down due to narrow therapeutic window of most of the compounds. A major reason for their poor clinical results is the consequence of dosing limitation caused by side effects such as nausea and emesis.[19] Recent findings in PDE4 knockout mice suggest that an inhibitor with PDE4B selectivity should retain many beneficial anti-inflammatory effects without the unwanted side effects[20,21].

The highly conserved catalytic domain of PDE4 isozymes makes the generation of inhibitors with PDE4 subtype selectivity a challenging task. However, residues in regulatory domain such as control region 3 (CR3) vary among subfamilies, which has proved to be responsible for PDE4B selectivity.[22]

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ORIGINAL ARTICLE

Insufficient Implementation of Tuberculosis Screening and Prophylaxis in Child Contacts: a Situational Analysis

J KROTZEK-SEAH[1], AB HIMAWAN[2], A RONDAGS[1,3], *JF METSEMAKERS[1], TRI NUR KRISTINA[2*]*

ABSTRACT

Background: Contact investigations and chemoprophylaxis are proven cost-effective and safe means to reduce TB-related morbidity and mortality in children living with pulmonary tuberculosis (PTB) cases.
Aim: To evaluate the implementation of tuberculosis (TB) screening and chemoprophylaxis in child contacts of smear-positive adult TB cases, and to identify practical barriers experienced by the staff of community health centers (CHCs) in a rural area in Central Java, Indonesia.
Methods: Firstly, a short questionnaire was used to collect information on whether children in the household were screened and received chemoprophylaxis through home visits or at the CHC. Secondly, semi-structured interviews and an FGD were performed with the TB officer, a nurse responsible for the TB program activities, the assistant of the TB officer, a medical doctor from the out-patient clinic, and the head of the CHC. The data was then independently analyzed using the theoretical thematic analysis, then the findings were compared and integrated into one set of themes.
Results: Out of 67 child contacts, determined through record reviews and visits of smear-positive TB patients, only 5(7.5%) were screened. None was started on chemoprophylaxis. In-depth interviews and a focus group discussion with CHCs' staff identified shortcomings in organization and management of care, lack of awareness and knowledge among staff, limited understanding of caregivers, and practical obstacles related to the rural setting.
Conclusions: A comprehensive approach is needed that matches these site-specific practical barriers and might require a redistribution of organizational power from health authorities to the CHCs.
Keywords: TB contact, children, screening, chemoprophylaxis

INTRODUCTION

It is only in recent years that more attention is drawn on the burden and impact of childhood tuberculosis (TB). Children usually get infected with the Mycobacterium tuberculosis by adult pulmonary TB (PTB) cases in their closest surroundings, i.e., parents or other household members. Particularly in children under 5 years of age (under-fives), bearing an underdeveloped immune system, the risk of progression to active disease after primary infection is high[1,2]. Contact investigations and chemoprophylaxis with isoniazid preventive therapy (IPT), are proven cost-effective and safe means to reduce TB-related morbidity and mortality in children living with PTB cases[3].[3]IPT can reduce the risk of developing active disease from primary (asymptomatic) infection by 60-65% over 2 years or longer[3].

In Indonesia, where TB remains a major public health challenge, 8.47% of the 328.824 newly diagnosed patients in 2012 were under the age of 15 years, exceeding the global average of 6% of TB cases that occur in children[4]. The Indonesian national TB control program (NTP) recommends screening of all child household contacts (in particular under-fives) of smear-positive PTB cases using the Indonesian scoring system for TB diagnosis in children[5].

Different from the WHO recommendations (Fig. 1), this scoring system requires tuberculin skin test (TST) and chest-X-ray (CXR). If TB disease is excluded (i.e. score <6), under-fives should receive a 6-month IPT (5-10 mg/kg bodyweight daily),[5]which in line with the present WHO recommendations[6] (Fig. 1). Current recommendations recommend 10mg/kg per day for 6 months[7].

A systematic review showed an overall prevalence of TB infection ranging from 24.4 to 69.2% in children (<15 years) living with a smear-positive TB case in South East Asia[8] Despite the benefits of screening and chemoprophylaxis in child contacts, numerous studies from high TB burden countries indicated that these measures are often poorly implemented[9-11]. A cross-sectional study in 4 TB units in South India, for example, showed that only 14% of 84 child contacts under 5 years had been screened for TB disease, and only 19% had been initiated on IPT with no follow-up. Focus group

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