https://doi.org/10.31925/farmacia.2025.2.22 **ORIGINAL ARTICLE**

THE IMPACT OF NAT2 POLYMORPHISM ON ISONIAZID BLOOD LEVELS AND LIVER ENZYME ELEVATION IN TUBERCULOSIS PATIENTS IN SURABAYA, INDONESIA

DIAN NATASYA RAHARDJO [1,2], MARIANA WAHJUDI [3], RATU AYU DEWI SARTIKA [4], JONATHAN JONATHAN [3], DHAMMIKO WONGGO [3], RETNOSARI ANDRAJATI [1]*

[1]*Faculty of Pharmacy, Universitas Indonesia, Depok, 16424, West Java, Indonesia*
[2]*Faculty of Pharmacy, University of Surabaya, Surabaya, 60293, East Java, Indonesia*
[3]*Master of Biotechnology, University of Surabaya, Surabaya, 60293, East Java, Indonesia*
[4]*Faculty of Public Health, Universitas Indonesia, Depok, 16424, West Java, Indonesia*

**corresponding author: andrajati@farmasi.ui.ac.id*

Manuscript received: November 2024

Abstract

Isoniazid is the most pharmacogenetically studied anti-tuberculosis (TB) drug. However, the NAT2 genotype profile and its impact on the treatment of TB patients in Surabaya, Indonesia, have not yet been discovered. The objective of this study was to examine the impact of NAT2 polymorphisms on isoniazid blood levels and liver enzymes (ALT/AST) during the intensive phase of TB treatment. In this cohort study, 51 TB patients from several Community Health Centres in Surabaya underwent blood sampling for pre-ALT/AST and DNA genotyping examinations on the first day of treatment. Isoniazid levels were measured by taking blood samples 2 hours after the drug administration, and post-ALT/AST values were obtained at the end of the 2nd month of the intensive phase of TB treatment. Nanopore sequencing was employed to genotype DNA using MinION Mk1B. ALT/AST exams were performed with the local clinical laboratory, and isoniazid levels were measured using high-performance liquid chromatography (HPLC). The predominant NAT2 genotypes observed in this study were NAT2*12A (43.14%), NAT2*6C (19.61%), and NAT2*12B (13.73%). Most TB patients in Surabaya possessed rapid acetylator phenotypes and low isoniazid blood levels. However, no correlation was observed between the NAT2 phenotype and the elevation of ALT/AST. In conclusion, NAT2 polymorphism influences the isoniazid blood levels but does not correlate with elevated ALT/AST following the intensive phase of TB treatment..

Rezumat

Izoniazida este cel mai intens studiat medicament tuberculostatic din perspectivă farmacogenetică. Cu toate acestea, profilul genotipurilor NAT2 și impactul acestora asupra tratamentului pacienților cu tuberculoză din Surabaya, Indonezia, nu au fost încă investigate. Scopul acestui studiu a fost de a evalua influența polimorfismelor genei NAT2 asupra nivelurilor plasmatice ale izoniazidei și asupra valorilor enzimelor hepatice (ALT/AST) în timpul fazei intensive a tratamentului anti-TB. În cadrul acestui studiu, 51 de pacienți cu tuberculoză provenind din mai multe centre de sănătate comunitare din Surabaya au fost supuși recoltării de probe de sânge pentru determinarea valorilor pretratament ale ALT/AST și pentru genotiparea ADN-ului în prima zi de tratament. Nivelurile de izoniazidă au fost măsurate prin recoltarea probelor de sânge la două ore după administrarea medicamentului, iar valorile post-tratament ale ALT/AST au fost obținute la sfârșitul celei de-a doua luni din faza intensivă a tratamentului. Genotiparea ADN-ului a fost realizată prin secvențiere de tip Nanopore, utilizând platforma MinION Mk1B. Analizele ALT/AST au fost efectuate în laboratorul clinic local, iar determinarea nivelurilor de izoniazidă s-a realizat prin cromatografie lichidă de înaltă performanță (HPLC). Cele mai frecvente genotipuri NAT2 identificate în acest studiu au fost NAT212A (43,14%), NAT26C (19,61%) și NAT2*12B (13,73%). Majoritatea pacienților cu tuberculoză din Surabaya au prezentat un fenotip de acetilatori rapizi și niveluri scăzute de izoniazidă în sânge. Totuși, nu s-a observat nicio corelație între fenotipul NAT2 și creșterea valorilor ALT/AST. În concluzie, polimorfismul genei NAT2 a influențat nivelurile sanguine ale izoniazidei, însă nu a fost corelat cu o creștere a valorilor ALT/AST în timpul fazei intensive a tratamentului tuberculostatic.

Keywords: NAT2 polymorphism, isoniazid, tuberculosis, liver enzyme

Introduction

Tuberculosis (TB) remains among the ten leading causes of mortality worldwide. According to the World Health Organization's study in 2022, the worldwide prevalence of TB is estimated to be at least 10 million individuals, with around 46% of TB cases concentrated in the Asian region. Indonesia is the second country with the most significant number of TB sufferers in the world, accounting for 10% of the global total [29]. Therapeutic failure and drug resistance in patients with drug-sensitive TB can happen because of insufficient levels of anti-TB drugs in the bloodstream. One factor that can contribute to this is the variability in drug metabolism, specifically the polymorphism of genes that encode drug metabolism.

Several studies have explored this relationship [1, 4, 6, 11, 13, 25]. Currently, INH has been the most extensively researched anti-TB drug in terms of pharmacogenetics. Some evidence recommends optimising the dosage based on genotype variations of INH-metabolizing enzymes [6, 9].

INH is converted to acetyl-INH by arylamine N-acetyltransferase 2 (NAT2), a protein with three distinct phenotypes: rapid-, intermediate-, and slow-acetylator [3]. Acetyl-INH is subsequently hydrolysed into a group of acetylhydrazine compounds, one of which is monoacetylhydrazine, which has been demonstrated to be hepatotoxic. Acetyl-INH is later re-acetylated by NAT2 to produce non-toxic diacetylhydrazine [5, 15, 27]. The acetylation status of TB patients is influenced by the presence of NAT2 genetic polymorphisms. Recent studies have demonstrated that NAT2 slow-acetylators are at a greater risk of experiencing hepatotoxic events caused by INH than rapid acetylators [3, 7, 15, 17, 20, 28, 30]. The slow acetylation process converts only a minor portion of monoacetylhydrazine to diacetylhydrazine, while the majority is oxidised to hepatotoxic compounds by CYP2E1 [5, 27].

The activity of the NAT2 enzyme is influenced by genetic variations in NAT2 that are present in humans. NAT2*4 is the wild-type allele with the highest NAT activity, while NAT2*5, NAT2*6, and NAT2*7 are alleles that decrease NAT activity [5, 15, 20]. The intermediate-acetylator type was the most prevalent type among TB patients in China and Japan, as indicated by the results of studies conducted in these countries. The slow-acetylator type was the second most prevalent type. In contrast, the slow-acetylator type dominates the TB population in India. The slow-acetylator type's presence in the TB population of the Asian continent has the potential to render this population susceptible to hepatotoxicity as a result of INH. In the meantime, the NAT2 gene in humans contains 36 variants that are the result of polymorphisms in single nucleotides (SNPs). Other studies are required from various ethnicities worldwide, as the susceptibility to hepatotoxicity is individual due to polymorphisms in the NAT2 gene [15].

This study used DNA sequencing to evaluate the correlation between INH blood levels and the NAT2 polymorphism in TB patients. This polymorphism was correlated to the treatment of TB patients concerning the occurrence of anti-TB adverse effects, specifically hepatotoxicity. Hepatotoxicity is evaluated by comparing ALT/AST (alanine aminotransferase/ aspartate aminotransferase) values before and after the intensive phase of treatment. The TB patients involved in this investigation were pulmonary TB patients who had recently undergone treatment at several Community Health Centres in Surabaya City, Indonesia.

Materials and Methods

Study design and sampling

This study used a cohort design involving TB patients as research subjects from several Community Health Centres in Surabaya City. The total sampling method was employed to collect the research subjects from all new TB patients in five Community Health Centres in Surabaya City who were treated between January and April 2023, met the inclusion criteria, and were willing to sign the informed consent form. The research subjects were to meet the following criteria: new cases of pulmonary TB, patients who had been confirmed positive for BTA through sputum examination, patients aged from adolescence to the elderly, and patients who were receiving first-line TB drugs, which included INH, rifampicin, pyrazinamide, and ethambutol. In the interim, subjects who are confirmed to be resistant to first-line anti-TB drugs, have a history of liver disease, are HIV-positive, and are unable to be contacted for monitoring during the intensive phase of treatment will be excluded.

Blood sampling

Blood samples were collected at time t = 0 prior to the administration of anti-TB drugs to assess pre-ALT/AST levels and DNA genotyping. Blood samples were collected using volumetric absorptive micro sampling (VAMS) at t = 2 hours after the patients had consumed anti-TB drugs to assess the INH blood levels. Subsequently, the patients were monitored for compliance during the two-month intensive treatment phase. Additional blood samples were taken at t = 60 days to ascertain the post-ALT/AST levels. The data were subsequently collected and statistically analysed.

DNA genotyping

The extraction of genomic DNA samples was conducted using the TIANamp Genomic DNA Kit from Tiangen. Afterwards, DNA sequencing was conducted utilising nanopore technology with the MinION Mk1B instrument from Oxford Nanopore Technologies®. The nucleotide sequence and NAT2 allele variants were analysed using the "EPI2ME" tool. The retrieved allele was utilised to predict the acetylator phenotype based on the database.

Determination of INH blood levels

INH blood levels were determined using an HPLC-MS/MS (high-performance liquid chromatography/ tandem mass spectrometry) apparatus. Three mL of blood samples were subjected to centrifugation at a speed of 3000 rpm, after which the serum was collected for subsequent processing. A straightforward extraction method was employed, involving protein precipitation using 150 µL of 15% trichloroacetic acid in 300 µL of serum. The mixture was vigorously stirred for 2 minutes and then spun at a speed of 3000 revolutions per minute for 10 minutes. Afterwards,

the supernatant was gathered, and 20 µL was introduced into the HPLC system. The stationary phase employed was a Novapak® C18 column with dimensions of 150 x 3.9 mm and a particle size of 3 microns. The mobile phase comprised a solution of 0.05 M sodium dihydrogen phosphate and acetonitrile at a ratio of 97:3. The mobile phase flowed at a rate of 1 mL/min at room temperature, and detection was performed at a wavelength of 280 nm.

Determination of Serum ALT/AST

The examination of ALT/AST liver enzymes was conducted in partnership with the local clinical laboratory using the kinetic enzymatic approach with the Sclavo Diagnostic Kit®. During the ALT examination, the GPT enzyme in the sample converts alanine into pyruvate and glutamate in the presence of 2-oxoglutarate. Pyruvate is converted into lactate and NAD in the presence of NADH and lactate dehydrogenase (LDH). The rate of NADH consumption, measured at a wavelength of 340 nm, is directly proportional to the concentration of ALT in the blood sample.

During the AST evaluation, when 2-oxoglutarate is present, aspartate is converted into oxalacetate and glutamate by the aspartate aminotransferase (AST/ GPT) found in the blood sample. Oxalacetate is converted into malate and NAD in the presence of NADH and malate dehydrogenase (MDH). The rate of NADH consumption, measured at a wavelength of 340 nm, is directly proportional to the concentration of AST in the blood sample.

Ethical considerations

This study was granted ethical authorisation by the Institutional Ethics Committee of the University of Surabaya. Furthermore, written informed consent ensured the subjects' personal information confidentiality and voluntary participation. The study was conducted in compliance with the ethical principles outlined in the Declaration of Helsinki and relevant local regulations involving human subject research.

Statistical analysis

Demographic data, the NAT2 gene polymorphism profile, INH blood levels, and ALT/AST levels were subjected to descriptive analysis and presented in frequency, mean, and standard deviation. The effect of acetylation type on the acquisition of INH blood levels and ALT/AST levels was analysed using bivariate analysis. Additionally, correlation analysis was conducted to investigate the relationship between alterations in ALT/AST levels and INH blood levels. IBM® SPSS Statistics version 27 was implemented for statistical analyses in this study.

Results and Discussion

The recruitment and observation of research subjects were carried out for six months from January 2023 to June 2023. The study was conducted at five Community Health Centres in Surabaya City and involved a total of 51 TB patients who were willing to participate as research subjects. Most of the research subjects were male patients (56.86%) with an age range of 19 - 44 years (52.94%) and a body weight between 38 and 54 kg (56.86%). Active smokers were present in 13.7% of the research subjects, and 11.8% had comorbidities of Diabetes Mellitus (Table I).

Table I

Characteristics of TB patients at Community Health Centres in Surabaya City

Characteristics	N	%	Mean ± SD (Min-Max)
Age (years)	51		
10 - 18	3	5.88	
19 - 44	27	52.94	42,04 ± 14.981 (15 - 74)
45 - 59	12	23.53	
≥ 60	9	17.65	
Weight (kg)	51		
30 - 37 kg	10	19.61	
38 - 54 kg	29	56.86	47.71 ± 10.975 (31 - 85)
55 - 70 kg	10	19.61	
≥ 71 kg	2	3.92	
Gender			
Male	29	56.86	
Female	22	43.14	
Comorbidities			
Diabetes Mellitus	6	11.8	
Smokers	7	13.7	

The comparative test results indicated that the achievement of INH levels in the blood would be influenced by smoking habits and gender. The results of this study indicated that female patients had higher INH blood levels than male patients (p = 0.02). Conversely, smokers had lower INH blood levels than non-smokers (p = 0.005) (Table II). However, the statistical results for other variables

did not indicate any association between INH blood levels and age, body weight, or dose (Table III). This suggests that there are other physiological factors that influence the metabolism of both male and female patients in addition to the variables examined in this study. Men generally have higher total body fluid, intracellular and extracellular fluid, total blood volume, plasma volume, and red blood cell volume than women. This condition leads to an increase in the distribution volume of drugs with water-soluble characteristics, such as INH, in men, which in turn results in a decrease in drug levels in the bloodstream [21]. The activity of the NAT2 enzyme, which is responsible for the metabolism of INH, can be induced by heterocyclic amine compounds in cigarettes, resulting in a decrease in INH blood levels in TB patients who smoke [24, 26].

Table II

Comparison of INH blood levels based on patient characteristics

Characteristics	INH blood levels (µg/mL) mean ± SD	p value
Gender		
Male	1.683 ± 1.383	0.020*
Female	2.009 ± 0.8819	
Comorbidities		
No comorbid	1.8596 ± 1.2648	0.715
Diabetes Mellitus	1.5550 ± 0.2848	
Smoking status		
Non-smokers	1.9605 ± 1.2274	0.005*
Smokers	0.9643 ± 0.2822	
INH Dose		
150 mg	1.8670 ± 1.1144	0.874^{+}
225 mg	1.7183 ± 1.0028	
300 mg	2.1640 ± 1.8219	
375 mg	1.4350 ± 0.4879	

* = $p < 0.05$ (Mann-Whitney Test); $^{+}$ = Kruskal-Wallis Test

Table III

Correlation of demographic characteristics and INH dose to INH blood levels

Characteristics	INH blood levels (µg/mL) (mean ± SD)	p value
INH dose (mg) (230.88 ± 55.810)	1.8237 ± 1.1937	0.882
Age (years) (42.04 ± 14.981)	1.8237 ± 1.1937	0.418
Body weight (kg) (47.71 ± 10.975)	1.8237 ± 1.1937	0.903

Spearman Correlation Test

The study findings reveal that the predominant genotype identified in TB patients in Surabaya is NAT2*12A, accounting for 43.14% of cases (Table IV). A separate study conducted in a different region of Indonesia examined 241 tuberculosis (TB) patients at Pasar Rebo Hospital in Jakarta and various TB clinics in Banten and West Java. The study revealed that the majority of patients possessed the NAT2*6A genotype, which is responsible for the slow acetylator type and is linked to the risk of drug-induced liver injury (DILI) [32]. This study's findings indicated that a significant proportion of TB patients exhibited the rapid acetylator phenotype. These patients had an average INH blood level of 1.446 ± 0.6432 µg/mL in their blood. The findings of this study contrast with previous research conducted in Indonesia, which indicated that the prevailing acetylator types in the country are intermediate and slow acetylator [16, 30, 31]. These results reveal novel polymorphism profiles in Indonesia since many TB patients in Surabaya exhibit a rapid acetylation type. The attainment of INH blood levels in patients with the rapid acetylator phenotype remains below the average attainment of INH levels in rapid acetylators in Japan, which is 2.22 ± 0.90 µg/mL [22]. However, it tends to be similar to the INH levels observed in rapid acetylators in West Sumatra, Indonesia, which are 1.25 µg/mL [18].

Compared to research conducted in other parts of Indonesia, this study reveals the wide range of NAT2 genotype variants found among TB patients in Indonesia. These findings provide supporting evidence for the necessity of implementing pharmacogenetic-based TB treatment in the country.

Polymorphism in the NAT2 gene arises from genetic changes in the form of mutations or single-nucleotide substitutions, also known as single-nucleotide polymorphisms (SNPs). The NAT2*12 allele family undergoes a mutation where a guanine base replaces adenine at the 803rd nucleotide position of the NAT2 gene sequence. This mutation results in an amino acid change from lysine to arginine at position

268. This alteration in the amino acid will impact the conformation of the protein and the catalytic function of NAT2. Whether the NAT2 activity increases or decreases will be determined by the interplay between the enzyme and the substrate. The NAT2*12 allele is characterized by a mutation that leads to an elevation in enzyme activity, resulting in the classification of the acetylator type as a quick acetylator. The majority of NAT2 alleles are haplotype alleles that contain many point mutations and one characteristic mutation. This mutant allele has the potential to destabilise the resultant protein and impact the functionality of the folded protein [19].

Table IV

Distribution of NAT2 genotype variants and prediction of acetylator phenotype

NAT2 Genotype	N (patient)	Frequency (%)	Phenotype	Frequency (%)
***4**	1	1.96	*Rapid*	60.78
***12A**	22	43.14	*Rapid*	
***12B**	7	13.73	*Rapid*	
***13A**	1	1.96	*Rapid*	
***5D**	5	9.80	*Slow*	33.33
***6A**	2	3.92	*Slow*	
***6C**	10	19.61	*Slow*	
***6F**	3	5.88	*Unknown*	5.88
Total	**51**	**100**		**100**

There is a substantial difference in INH blood levels between the rapid and slow acetylator types, according to Table V. This study's discovery of the NAT2*6F genotype with the unknown acetylator type suggests that NAT2 has a genetic variant whose effect on isoniazid metabolism is not entirely understood. However, the interim hypothesis that can be accepted for this study is that the NAT2*6F genotype tends to lead to the rapid acetylator type, based on the analysis results indicating no significant difference between INH blood levels in the rapid and unknown acetylator types. To determine and comprehend the functional mechanism of polymorphism in the unknown acetylator type, further investigation is still required. The study's findings suggest that the type of acetylator used will influence the attainment of INH levels. NAT2 will acetylate INH to acetylisoniazid, which will then hydrolyse to acetylhydrazine. NAT2 will then re-acetylate INH to a non-toxic diacetylhydrazine. Compared to the slow acetylator type, the rapid acetylator type causes INH to be acetylated to acetylisoniazid more quickly, resulting in lower blood levels of INH. Studies conducted by Perwitasari *et al.*, Wahyudi and Soedarsono, and Huang showed that the rapid acetylator type lowers the amount of INH in the blood by converting it to acetylisoniazid more quickly [5, 15, 27]. However, the average INH blood levels of the rapid and slow acetylator types in this investigation did not approach the therapeutic range of 3 - 6 µg/mL. This suggests that, besides the type of acetylator, other factors like age, body weight, gender, and how drugs are distributed in tissues may also affect how much INH is in the blood [8, 12].

Table V

Association of acetylator type with INH blood levels

Acetylator type	INH blood levels (µg/mL) (Mean ± SD) (Min - Max)	p value between groups	p value
Rapid	1.446 ± 0.6432 (0.41 - 2.81)	1	0.0387*
Slow	2.595 ± 1.626 (0.83 - 6.8)	0.0230*	
Unknown	1.360 ± 0.8246 (0.41 - 1.89)	0.9999	

* = $p < 0.05$ (Kruskal-Wallis Test, Dunn's multiple comparisons)

Table VI

Comparison of ALT and AST values pre- and post-intensive phase

Parameter	Mean ± SD (U/L) (Min - Max)	p value
AST		
pre	18.22 ± 6.4072 (4 - 40)	0.021*
post	25.90 ± 13.3045 (11 - 78)	
ALT		
pre	16.02 ± 10.8213 (6 - 82)	0.0000*
post	23.90 ± 14.2116 (10 - 86)	

* = $p < 0.05$ (paired t-test)

The comparative test findings revealed a significant disparity in ALT and AST values before and after the intensive phase of TB treatment, as shown in Table VI. ALT and AST levels may rise in TB patients as a result of INH usage. This increase can begin as early as one week after starting the medication and continue for up to six months of treatment. However, it is possible for liver function to remain normal without any drug-induced liver injury (DILI) occurring, even without adjusting the dosage of isoniazid. This phenomenon is referred to as the liver's adaptability [2, 10]. Hence, this study

examined the alterations in AST and ALT levels as indicators of isoniazid side effects.

The analytical results indicated that variations in acetylator types did not have an impact on alterations in ALT and AST levels. However, it was observed that INH blood levels were positively associated with elevated ALT and AST levels following a two-month intensive phase of TB treatment (Table VII). This study did not observe any negative consequences of drug-induced liver damage (DILI) since none of the patients exhibited alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels that exceeded three times the upper limit of normal (ULN). The patient's INH blood levels, averaging 1.8237 ± 1.1937 (μg/mL), were below the therapeutic range of 3-6 μg/mL. This suggests that the INH levels in the patient's blood did not reach a concentration that could cause hepatotoxicity [14]. Furthermore, according to observations made on several patients, acetylcysteine, a substance with recognised hepatoprotective properties [23], was also prescribed to the patients.

Table VII

The impact of acetylator type and INH blood levels on changes in AST and ALT levels after the intensive phase of TB treatment

Parameter	Changes in AST (Mean ± SD (U/L)	p value	Changes in ALT (Mean ± SD (U/L)	p value
INH blood levels	7.6863 ± 12.7726	0.000*	7.8824 ± 12.6691	0.000*
Rapid acetylator	5.7353 ± 9.2091	0.246^{+}	6.0588 ± 11.5364	0.082^{+}
Slow acetylator	11.5882 ± 17.6248		11.5294 ± 14.3489	

Note: * = $p < 0.05$ (Spearman correlation test), $^{+}$ Mann Whitney test

Conclusions

This study demonstrates that NAT2 polymorphism impacts INH blood levels but does not result in alterations in ALT/AST levels of TB patients. According to the study's findings, the blood levels of INH in all TB patients who participated did not approach the INH therapeutic range for both rapid and slow acetylator types. This explains why none of the patients experienced any hepatotoxic side effects.

Acknowledgement

This research was supported by ”Hibah Publikasi Terindeks Internasional (PUTI) Pascasarjana 2023, Universitas Indonesia” Number: NKB-036/UN2.RST/HKP.05.00/2023.

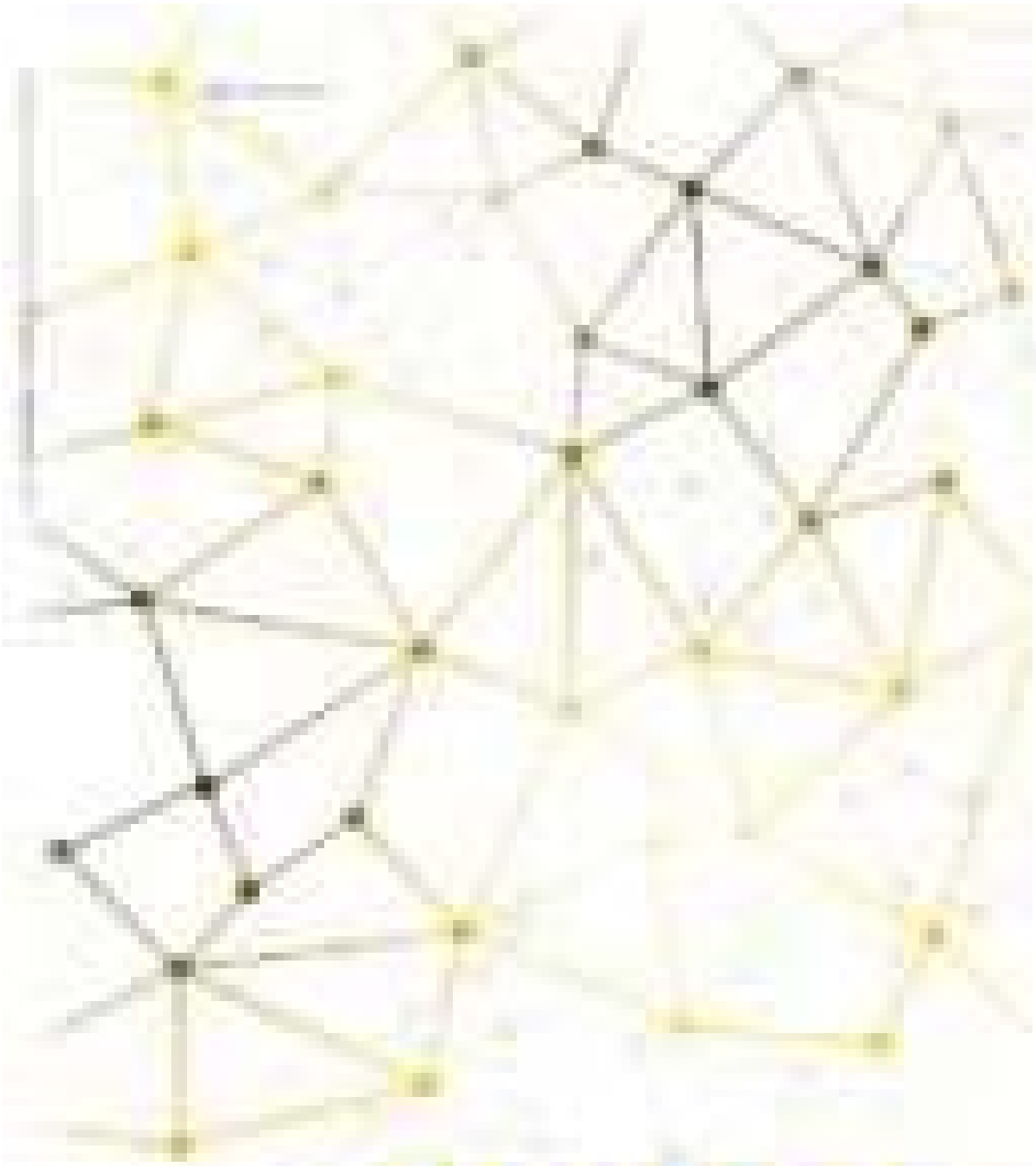
Conflict of interest

The authors declare no conflict of interest.

References

1. Butnaru T, Mihălțan FD, Constantin AA, Quality of life of Romanian patients with sensitive and drug-resistant tuberculosis during and after treatment. *Farmacia*, 2024; 72(3): 675-687.
2. Chalasani N, Bonkovsky HL, Fontana R, Lee W, Stolz A, Talwalkar J, Reddy KR, Watkins PB, Navarro V, Barnhart H, Gu J, Serrano J, Ahmad J, Bach N, Bansal M, Barnhart HX, Beavers K, Calvo FO, Chang C, Conjeevaram H, Conner G, Darling J, De Boer Y, Dieterich D, Dipaola F, Durazo FA, Everhart JE, Fontana RJ, Ghabril MS, Goldstein D, Gopalreddy V, Grewal P, Hayashi PH, Hoofnagle J, Kaplowitz N, Liangpunsakul S, Lichtman S, Liu L, Navarro VJ, Odin J, Rossi S, Russo M, Schiano T, Sherker AH, Vuppalanchi R, Zacks S, Balasco A, Chesney K, Corne A, Cummings S, Groseclose G, Hammett A, Hooker J, Kesar V, Mao S, Marks K, McFadden R, Melgoza Y, Mikhail S, Milstein S, Morlan W, Peacock V, Rosado N, Russell T, Vega M, Verma M, Walker P, Yalamanchili R, McClanahan-Crowder M, Galan K, Chau T, Ragavan K, Rostami H, Puglisi-Scharenbroich C, Torrance RJ, Van Raaphorst R, Features and Outcomes of 899 Patients With Drug-Induced Liver Injury: The DILIN Prospective Study. *Gastroenterology*, 2015; 148(7): 1340-1352.e7.
3. Du H, Chen X, Fang Y, Yan O, Xu H, Li L, Li W, Huang W, Slow N-acetyltransferase 2 genotype contributes to anti-tuberculosis drug-induced hepatotoxicity: A meta-analysis. *Mol Biol Rep.*, 2013; 40(5): 3591-3596.
4. Heysell SK, Moore JL, Keller SJ, Houpt ER, Therapeutic drug monitoring for slow response to tuberculosis treatment in a state control program, Virginia, USA. *Emerg Infect Dis.*, 2010; 16(10): 1546-1553.
5. Huang YS, Recent progress in genetic variation and risk of antituberculosis drug-induced liver injury. *J Chin Med Assoc.*, 2014; 77(4): 169-173.
6. Jung JA, Kim TE, Lee H, Jeong BH, Park HY, Jeon K, Jung Kwon O, Ko JW, Choi R, Woo HI, Koh WJ, Lee SY, A proposal for an individualized pharmacogenetic-guided isoniazid dosage regimen for patients with tuberculosis. *Drug Des Devel Ther.*, 2015; 9: 5433-5438.
7. Lee SW, Chung LSC, Huang HH, Chuang TY, Liou YH, Wu LSH, NAT2 and CYP2E1 polymorphisms and susceptibility to first-line anti-tuberculosis drug-induced hepatitis. *Int J Tuberc Lung Dis.*, 2010; 14(5): 622-626.
8. Lei Q, Wang H, Zhao Y, Dang L, Zhu C, Lv X, Wang H, Zhou J, Azim A, Determinants of serum concentration of first-line anti-tuberculosis drugs from China. *Medicine*, 2019; 98: 41.

9. McIlleron H, Chirehwa MT, Current research toward optimizing dosing of first-line antituberculosis treatment. *Expert Rev Anti Infect Ther.*, 2019; 17(1): 27-38.
10. Metushi I, Uetrecht J, Phillips E, Mechanism of isoniazid-induced hepatotoxicity: then and now. *Br J Clin Pharmacol.*, 2016; 81(6): 1030-1036.
11. Park JS, Lee JY, Lee YJ, Kim SJ, Cho YJ, Yoon H Il, Lee CT, Song J, Lee JH, Serum levels of antituberculosis drugs and their effect on tuberculosis treatment outcome. *Antimicrob Agents Chemother.*, 2016; 60(1): 92-98.
12. Parkin DP, Vandenplas S, Botha FJH, Vandenplas ML, Seifart HI, Van Helden PD, Van Der Walt BJ, Donald PR, Van Jaarsveld PP, Trimodality of isoniazid elimination - Phenotype and genotype in patients with tuberculosis. *Am J Respir Crit Care Med.*, 1997; 51(11): 1053-1054.
13. Pasipanodya JG, Srivastava S, Gumbo T, Meta-analysis of clinical studies supports the pharmacokinetic variability hypothesis for acquired drug resistance and failure of antituberculosis therapy. *Clin Infect Dis.*, 2012; 55(2): 169-177.
14. Perumal R, Naidoo K, Naidoo A, Padayatchi N, Clinical impact of plasma concentrations of first-line antituberculosis drugs. *S Afr Med J.*, 2023; 113(3): 148-153.
15. Perwitasari DA, Atthobari J, Wilffert B, Pharmacogenetics of isoniazid-induced hepatotoxicity. *Drug Metab Rev.*, 2015; 47(2): 222-228.
16. Perwitasari DA, Darmawan E, Mulyani UA, Van Der Vlies P, Alffenaar JC, Atthobari J, Wilffert B, Polymorphisms of NAT2, CYP2E1, GST, and HLA Related to Drug-Induced Liver Injury in Indonesian Tuberculosis Patients. *Int J Mycobacteriol.*, 2018; 7(4): 380-386.
17. Richardson M, Kirkham J, Dwan K, Sloan DJ, Davies G, Jorgensen AL, NAT2 variants and toxicity related to anti-tuberculosis agents: A systematic review and meta-analysis. *Int J Tuberc Lung Dis.*, 2019; 23(3): 293-305.
18. Senja M, Basyar M, Sabri YS, Afriani A, Correlation between N-Acetyltransferase 2 (NAT2) Polymorphism Genotype with Plasma Isoniazid (INH) Concentration in MDR TB Patients Receiving Short Regimen in West Sumatera. *J Respir Indo.*, 2022; 42(1): 26-33.
19. Sim E, Abuhammad A, Ryan A, Arylamine N-acetyltransferases: from drug metabolism and pharmacogenetics to drug discovery. *Br J Pharmacol.*, 2014; 171(11): 2705-2725.
20. Singla N, Gupta D, Birbian N, Singh J, Association of NAT2, GST and CYP2E1 polymorphisms and anti-tuberculosis drug-induced hepatotoxicity. *Tuberculosis*, 2014; 94(3): 293-298.
21. Soldin OP, Mattison DR, Sex Differences in Pharmacokinetics and Pharmacodynamics. *Clin Pharmacokinet.*, 2009; 48(3): 143-157.
22. Sotsuka T, Sasaki Y, Hirai S, Yamagishi F, Ueno K, Association of isoniazid-metabolizing enzyme genotypes and isoniazid-induced hepatotoxicity in tuberculosis patients. *In Vivo*, 2011; 25(5): 803-812.
23. Sukumaran D, Usharani P, Paramjyothi GK, Subbalaxmi MVS, Sireesha K, Abid Ali M, A study to evaluate the hepatoprotective effect of N-acetylcysteine on anti tuberculosis drug induced hepatotoxicity and quality of life. *Indian J Tuberc.*, 2023; 70(3): 303-310.
24. Teleka S, Jochems SHJ, Jirström K, Stocks T, The interaction between smoking and bladder cancer genetic variants on urothelial cancer risk by disease aggressiveness. *Cancer Med.*, 2022; 11(15): 2896-2905.
25. Um SW, Lee SW, Kwon SY, Yoon HI, Park KU, Song J, Lee CT, Lee JH, Low serum concentrations of anti-tuberculosis drugs and determinants of their serum levels. *Int J Tuberc Lung Dis.*, 2007; 11(9): 972-978.
26. Voutsinas J, Wilkens LR, Franke A, Vogt TM, Yokochi LA, Decker R, Le Marchand L, Heterocyclic amine intake, smoking, cytochrome P450 1A2 and N-acetylation phenotypes, and risk of colorectal adenoma in a multiethnic population. *Gut*, 2013; 62(3): 416-422.
27. Wahyudi AD, Soedarsono S, Hepatotoxicity Pharmacogenomic of Anti Tuberculosis Drugs. *Jurnal Respirasi*, 2015; 1(3): 103-108.
28. Wang PY, Xie SY, Hao Q, Zhang C, Jiang BF, NAT2 polymorphisms and susceptibility to anti-tuberculosis drug-induced liver injury: A meta-analysis. *Int J Tuberc Lung Dis.*, 2012; 16(5): 589-595.
29. WHO, Global Tuberculosis Report 2023. World Health Organization: Geneva, Swiss, 2023; 2-29.
30. Yuliwulandari R, Prayuni K, Susilowati RW, Subagyo S, Soedarsono S, M Sofro AS, Tokunaga K, Shin JG, NAT2 slow acetylator is associated with anti-tuberculosis drug-induced liver injury severity in Indonesian population. *Pharmacogenomics*. 2019; 20(18): 1303-1310.
31. Yuliwulandari R, Susilowati RW, Razari I, Viyati K, Umniyati H, Prayuni K, N-acetyltransferase 2 polymorphism and acetylation profiles in Buginese ethnics of Indonesia. *Ann Hum Genet.*, 2019; 83(6): 465-471.
32. Yuliwulandari R, Susilowati RW, Wicaksono BD, Viyati K, Prayuni K, Razari I, Kristin E, Syafrizal, Subagyo, Sri Diana E, Setiawati S, Ariyani A, Mahasirimongkol S, Yanai H, Mushiroda T, Tokunaga K, NAT2 variants are associated with drug-induced liver injury caused by anti-tuberculosis drugs in Indonesian patients with tuberculosis. *J Hum Genet.*, 2016; 61(6): 533-537.



FARMACIA

Editorial Board

Current Issue

Volume 73 | Number 2

Year 2025

Table of Contents

Cover

Search Archive

Keywords...

Advanced search

Search

Search Archive

DIAN

Advanced search

Search

Farmacia Journal 2/2025

Volume 73 | Number 2 | Year 2025

Download this issue's covers, and announcements

Download Full Article PDF

6. **THE ROLE OF IL-6 AND IL-1 IN COVID-19 DISEASE PROGRESSION: THE IMPACT OF GENDER-BASED DIFFERENCES, BMI VARIABILITY AND CO-MEDICATIONS**

AIDA-ISABELA ADAMESCU 1,2, CĂTĂLIN TILIȘCAN 1,2*, LAURENȚIU MIHĂIȚĂ STRATAN 1,2, NICOLETA MIHAI 1,2, OANA-ALEXANDRA GANEA 1,2, VICTOR DANIEL MIRON 1,2, SEBASTIAN CIOBANU 1,3, VICTORIA ARAMĂ 1,4, ȘTEFAN SORIN ARAMĂ 1,2

1 "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania
2 "Matei Balș" National Institute of Infectious Diseases, Bucharest, Romania
3 Emergency University Hospital, Bucharest, Romania
4 "Alessandrescu Rusescu" National Institute for Mother and Child Care, Bucharest, Romania

Download Full Article PDF

7. **THE INFLUENCE OF MORINGA OLEIFERA OIL ON NEUROBLASTOMA BASAL OXIDATIVE STRESS, INFLAMMATION AND AUTOPHAGY MECHANISM**

SOHAIR ALY HASSAN 1, RAMESA SHAFI BHAT 2*, ABEER AL-DBASS 2, ARWA ISHAQ A KHAYYAT 3, AFAF AL ANSARY 4

1 Therapeutic Chemistry Department, Pharmaceutical Industries Research Institute, National Research Centre, Cairo, Egypt
2 Department of Biochemistry, College of Science, King Saud University, Riyadh, Kingdom of Saudi Arabia
3 Genome Research Chair, Department of Biochemistry, College of Science, King Saud University
4 Autism Centre, Lotus Holistic Alternative Medical Canter, Abu Dhabi

Download Full Article PDF

8. **FORMULATION AND CHARACTERISATION OF PLGA-DOXORUBICIN COMPOSITES CONJUGATED WITH BISPHOSPHONATES IN ONCOLOGICAL THERAPY**

ROBERTO-ANGELO POSTELNICU 1, MARIA-VIORICA CIOCÎLTEU 1*, COSTEL VALENTIN MANDA 1, ROXANA-MARIA BĂLĂȘOIU 1, SILVIA ANDREEA PÎRVU 1, GABRIELA RĂU 1, CLAUDIU NICOLICESCU 2, ANDREEA GABRIELA MOCANU 1, JOHNY NEAMȚU 1

1 Faculty of Pharmacy, University of Medicine and Pharmacy 2 Petru Rareș Street, 200349, Craiova, Dolj County, Romania
2 Faculty of Mechanics, University of Craiova, 1 Călugăreni Street, 220037, Drobeta Turnu-Severin, Mehedinţi County, Romania

Download Full Article PDF

9. **TETRADECYL MALTOSIDE AND DIMETHYL-PALMITOYL- AMMONIO-PROPANE-SULFONATE AS EFFECTIVE PERMEATION ENHANCERS FOR SALMON CALCITONIN AND PRAMLINTIDE: A COMPARATIVE IN VITRO STUDY ON CACO-2 CELL LINES**

ANDREI HAMZA 1, RĂZVAN-MIHAI PRISADA 2*, GABRIEL ȘARAMET 1

"Carol Davila" University of Medicine and Pharmacy, Faculty of Pharmacy, 37 Dionisie Lupu Street, Bucharest, 020021, Romania
1 Department of Pharmaceutical Technology and Biopharmacy
2 Department of Physical and Colloidal Chemistry

Download Full Article PDF

10. **EXPLORING THE THERAPEUTIC POTENTIAL OF SOUR CHERRY LEAF EXTRACT (PRUNUS CERASUS L.): A COMPREHENSIVE IN VITRO AND IN VIVO EVALUATION**

CHAIMA MAMOUN 1, FATIMA ZAHRA GHANEMI 1*, NABILA YELLES 2, FATIMA ZOHRA CHENNI 3, RYM ESSID 4, DANISH PATOLI 5, IMAD ABDELHAMID EL HACI 1,6, KADDOUR BENARIBA 1, ASMAA RAHMOUN 1, OMAR KHAROUBI 7, MERIEM BELARBI 1, OLFA TABBENE 4

1 Laboratory of Natural Products « LAPRONA », Department of Biology, Abou Bakr Belkaid University, Tlemcen. Algeria

4 Laboratory of Bioactive Substances, Biotechnology Center of Borj-Cedria Technopole, BP 901, 2050 Hammam-Lif, Tunisia
5 Faculty of Pharmacy, Liaquat University of Medical and Health Sciences (LUMHS), Jamshoro, Sindh, Pakistan
6 Center of Scientific and Technical Research in Physico-Chemical Analysis (CRAPC), Bou-Ismail, Tipaza, Algeria
7 Laboratory of Biotoxicology Experimentale, Biodepollution and Phytoremediation, Faculty of Life and Natural Sciences, University Oran1, Oran, Algeria

Download Full Article PDF

11. ETHANOLIC EXTRACT OF JUNIPERUS COMMUNIS EXHIBITS ANTIMICROBIAL ACTIVITY AND SELECTIVE CYTOTOXICITY IN PANC-1 CANCER CELLS COMPARED TO HEPARG HEPATOCYTES

CRISTINA DAN 1#, BOGDAN ALMAJAN-GUTA 2#, ALINA ARABELA JOJIĆ 3,4*, STEFANIA- IRINA DUMITREL 3,5, IASMINA-ALEXANDRA PREDESCU 3,5, DIANA-SIMONA TCHIAKPE- ANTAL 3,4,5, ANDREEA SMEU 3,5, ROBERT JIJIE 3,5, IOANA IONITA 6,7, ANA-CRISTIANE DRAGOMIR 1, SIMONA ARDELEAN 8, ADRIANA DĂRĂBAN 8

1 Doctoral School, "Victor Babeș" University of Medicine and Pharmacy, 300041, Timișoara, Romania
2 Department of Physical Therapy and Special Motricity, West University of Timișoara, 300223, Timișoara, Romania
3 Faculty of Pharmacy, "Victor Babeș" University of Medicine and Pharmacy, 2 Eftimie Murgu Square, 300041, Timișoara, Romania
4 Department of Pharmaceutical Botany, Faculty of Pharmacy, "Victor Babeș" University of Medicine and Pharmacy Timișoara, 2 Eftimie Murgu Square, 300041, Timișoara, Romania
5 Research Centre for Pharmacotoxicologic Evaluations (FARMTOX), "Victor Babeș" University of Medicine and Pharmacy Timișoara, 2 Eftimie Murgu Square, 300041, Timișoara, Romania
6 First Department of Internal Medicine, "Victor Babeș" University of Medicine and Pharmacy, 300041, Timișoara, Romania
7 Department of Haematology, Emergency Municipal Hospital Timișoara, 300041, Timișoara, Romania
8 Faculty of Pharmacy, "Vasile Goldiș" Western University of Arad, 94 Revoluției Boulevard, 310130, Arad, Romania

Download Full Article PDF

12. IMPLEMENTATION OF AN ANTIBIOTIC RESTRICTION FORMULARY AND THE IMPACT ON CONSUMPTION IN A ROMANIAN HOSPITAL: A THREE-YEAR RETROSPECTIVE STUDY

SORINA HÎNCU 1,2#, MIRUNA-MARIA APETROAEI 1*, MIHAELA CRISTINA NEGULESCU 1,2, ALEXANDRU BLIDARU 1#, MANUELA GHICA 1, DENISA IOANA UDEANU 1,3

1 "Carol Davila" University of Medicine and Pharmacy, 6 Traian Vuia Street, 020956, Bucharest, Romania
2 "Fundeni" Clinical Institute, 258 Fundeni Street, 022328, Bucharest, Romania
3 "Marius Nasta" Institute of Pneumophthisiology, 90 Viilor Street, 050159, Bucharest, Romania

Download Full Article PDF

13. NEW PERSPECTIVES IN THE ANTIMICROBIAL POTENTIAL OF THYME AND OREGANO ESSENTIAL OILS

NELI ERMENLIEVA 1, SYLVIA STAMOVA 2*, GABRIELA TSANKOVA 1, EMILIA GEORGIEVA 3

1Department of Microbiology and Virusology, Faculty of Medicine, Medical University, Varna, Bulgaria
2Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Medical University, Varna, Bulgaria
3Training Sector "Medical Laboratory Technician", Medical College, Medical University, Varna, Bulgaria

Download Full Article PDF

14. GLYCAEMIC CONTROL IN PAEDIATRIC TYPE 1 DIABETES: THE INTERPLAY OF DIABETES ACCEPTANCE AND MEDICAL TECHNOLOGIES

DENISA MARIN-BATIR 1#, ALINA DELIA POPA 2#, MONICA HANCIANU 3*, ANDREEA- MARIA MITRAN 3, SILVIA ROBU 1, IOANA MITA-BACIU 2, RIANA HUZUM 2, IONUT-IULIAN LUNGU 3, CORNELIA MIRCEA 3, AUREL NECHITA 1, OANA CIOANCA 3

1 Faculty of Medicine and Pharmacy, "Dunarea de Jos" University, 35 Al. I. Cuza Street, 800216 Galati, Romania
2 Faculty of Medicine, "Grigore T. Popa" University of Medicine and Pharmacy, 700115 Iasi, Romania
3 Faculty of Pharmacy, "Grigore T. Popa" University of Medicine and Pharmacy, 700115 Iasi, Romania

Download Full Article PDF

15. THERAPEUTIC EFFECT OF COMBINED ULINASTATIN AND GLUTAMINE

XIU YANG, YANJUN WEI, HUA LI, KE XU, GUANGRONG YE, YAN ZHANG, TAO LU, JUAN YAN, JIABING PENG, GE ZHANG *

Department of Critical Care Medicine, The First People's Hospital of Longquanyi District, Chengdu, 610100, China

Download Full Article PDF

16. **ENHANCING MICROFRACTURE TREATMENT FOR CHONDRAL LESIONS WITH PLATELET-RICH PLASMA: AN OBSERVATIONAL STUDY**

ANDREI VISOIANU 1,2*, GABRIELA SOARE 1,2, COSMIN CONSTANTIN BACIU 1,2, RAZVAN ENE 1,2, GHEORGHE ION POPESCU 1,2

1 Clinical Emergency Hospital Bucharest, Romania
2 "Carol Davila" University of Medicine and Pharmacy Bucharest, Romania

Download Full Article PDF

17. **EXPLORING THE ANTI-FATIGUE EFFECTS OF WATERMELON RIND: A NATURAL BOOST FOR ENDURANCE**

MUKTI PRIASTOMO 1, AMIRAH ADLIA 2*, SAMSUL BAHRI 3, ROHAYATI 1, VALENTINA LUMBANTOBING 1, I KETUT ADNYANA 1

1 Department of Pharmacology and Clinical Pharmacy, School of Pharmacy, Institut Teknologi Bandung, Bandung Indonesia
2 Department of Pharmaceutical Pharmacy, School of Pharmacy, Institut Teknologi Bandung, Bandung Indonesia
3 Department of Sport Science, School of Pharmacy, Institut Teknologi Bandung, Bandung Indonesia

Download Full Article PDF

18. **DEVELOPMENT OF HIGH-THROUGHPUT NIR-CHEMOMETRIC METHODS FOR THE CHARACTERISATION OF POWDER BLENDS FOR TABLETTING AND EXTENDED-RELEASE TABLETS WITH KETOPROFEN**

TIBOR CASIAN 1, ANDRA REZNEK 1, LUCIA MARIA RUS 2*, ANDREEA LOREDANA VONICA-ȚINCU 3, RAREȘ IOVANOV 1, IOAN TOMUȚĂ 1

1 Department of Pharmaceutical Technology and Biopharmacy, Faculty of Pharmacy, "Iuliu Haţieganu" University of Medicine and Pharmacy, 41 Victor Babeș Street, Cluj-Napoca, Romania
2 Department of Drug Analysis, Faculty of Pharmacy, "Iuliu Haţieganu" University of Medicine and Pharmacy, 6 Louis Pasteur Street, Cluj-Napoca, Romania
3 Department of Preclinical Medicine, Faculty of Medicine, "Lucian Blaga" University, 2A Lucian Blaga Street, Sibiu, Romania

Download Full Article PDF

19. **SYNERGISTIC EFFECTS OF FLUCONAZOLE AND ROSMARINUS OFFICINALIS ESSENTIAL OIL AGAINST CANDIDA SPP. STRAINS**

MARINA IONELA NEDEA (ILIE) 1, IOANA-CRISTINA MARINAȘ 2*, MIHAELA BULEANDRA 3, DANA MARIA MUNTEAN 4, SILVIU CONSTANTIN BĂDOIU 1, MĂDĂLINA SOLOMON 1,5, OANA POPESCU 5, DRAGOȘ ȘERBAN 1, ANA MARIA DASCĂLU 1, CORNELIU TUDOR 1, ANDREEA LETIȚIA ARSENE 1,5, BRUNO ȘTEFAN VELESCU 1, IRINA GHEORGHE-BARBU 2,6

1 "Carol Davila" University of Medicine and Pharmacy, 37 Dionisie Lupu Street, 020021, Bucharest, Romania
2 The Research Institute of the University of Bucharest (ICUB), 050095, Bucharest, Romania
3 Department of Analytical Chemistry, Faculty of Chemistry, University of Bucharest, 90-92 Panduri Avenue, 050663, Bucharest, Romania
4 Department of Pharmaceutical Technology and Biopharmacy, Faculty of Pharmacy, "Iuliu Haţieganu" University of Medicine and Pharmacy, 8 Victor Babeș Street, 400012, Cluj-Napoca, Romania
5 "Marius Nasta" Pneumophthisiology Institute, 90 Viilor Road, 050159, Bucharest, Romania
6 Faculty of Biology, University of Bucharest, 1-3 Intrarea Portocalelor, 060101, Bucharest, Romania

Download Full Article PDF

20. **SYSTEM PHARMACOLOGY AND MOLECULAR MODELLING TO IDENTIFY POTENTIAL DRUG CANDIDATES FROM THE SOPHORA PLANT GENUS FOR CHRONIC BRONCHITIS TREATMENT**

MUNAZZAH MALIK 1, MIAN MUHAMMAD MUBASHER 2, ISHA ZAFAR 1,

1 Centre for Applied Molecular Biology, University of the Punjab, Lahore, Pakistan
2 Department of Information Technology, University of the Punjab, Lahore, Pakistan
3 Department of Plant Breeding and Genetics, Faculty of Agricultural Sciences, University of the Punjab, Lahore, Pakistan
4 Department of Clinical Pharmacy, College of Pharmacy, King Saud University, 11451 Riyadh, Saudi Arabia
5 School of Biological Sciences and Technology, Liupanshui Normal University, Liupanshui 55300, China

Download Full Article PDF

21. MYRICETIN-FISETIN COMBINATORIAL TREATMENT AS A POTENTIAL STRATEGY FOR CUTANEOUS MELANOMA – AN IN VITRO STUDY

CRISTINA GROSU (DUMITRESCU) 1,2#, MIHAELA BOȚA 3#, DIANA BONȚE 4*, CLAUDIA TOMA 5, ANDREEA SMEU 1,2, LAVINIA VLAIA 3, CASIANA BORU 5

1 Discipline of Toxicology, Drug Industry, Management and Legislation, Faculty of Pharmacy, "Victor Babeș" University of Medicine and Pharmacy Timișoara, 2 Eftimie Murgu Square, 300041, Timișoara, Romania
2 Research Centre for Pharmaco-Toxicological Evaluation, Faculty of Pharmacy, "Victor Babeș" University of Medicine and Pharmacy, 2 Eftimie Murgu Square, 300041, Timișoara, Romania
3 Department II-Pharmaceutical Technology, Faculty of Pharmacy, "Victor Babeș" University of Medicine and Pharmacy, 2 Eftimie Murgu Square, 300041, Timișoara, Romania
4 Discipline of Biochemistry, Department IV, "Victor Babeș" University of Medicine and Pharmacy, Timișoara, Romania
5 "Vasile Goldiș" Western University of Arad, Romania, 86 Liviu Rebreanu Street, 310048, Arad, Romania

Download Full Article PDF

22. THE IMPACT OF NAT2 POLYMORPHISM ON ISONIAZID BLOOD LEVELS AND LIVER ENZYME ELEVATION IN TUBERCULOSIS PATIENTS IN SURABAYA, INDONESIA

DIAN NATASYA RAHARDJO 1,2, MARIANA WAHJUDI 3, RATU AYU DEWI SARTIKA 4, JONATHAN JONATHAN 3, DHAMMIKO WONGGO 3, RETNOSARI ANDRAJATI 1*

1Faculty of Pharmacy, Universitas Indonesia, Depok, 16424, West Java, Indonesia 2Faculty of Pharmacy, University of Surabaya, Surabaya, 60293, East Java, Indonesia 3Master of Biotechnology, University of Surabaya, Surabaya, 60293, East Java, Indonesia 4Faculty of Public Health, Universitas Indonesia, Depok, 16424, West Java, Indonesia

Download Full Article PDF

23. ENHANCING THE DISSOLUTION RATE OF TICAGRELOR THROUGH PREPARATION WITH CYCLODEXTRINS – TABLET FORMULATION AND EVALUATION

LOREDANA-MARIA MARIN 1*, EMMA-ADRIANA OZON 2, VALENTINA ANUȚA 3, IULIAN SÂRBU 4, SÎNZIANA OPRIȚESCU 5, MARCIN SKOTNICKI 6, JANINA LULEK 6, DOINA DRĂGĂNESCU 1

1 "Carol Davila" University of Medicine and Pharmacy, Faculty of Pharmacy, Department of Pharmaceutical Physics, 020956, Bucharest, Romania
2 "Carol Davila" University of Medicine and Pharmacy, Faculty of Pharmacy, Department of Pharmaceutical Technology and Biopharmacy, 020956, Bucharest, Romania
3 "Carol Davila" University of Medicine and Pharmacy, Faculty of Pharmacy, Department of Physical and Colloidal Chemistry, 020956, Bucharest, Romania
4 "Carol Davila" University of Medicine and Pharmacy, Faculty of Pharmacy, 020956, Bucharest, Romania
5 "Carol Davila" University of Medicine and Pharmacy, Faculty of Pharmacy, Department of Clinical Laboratory and Food Safety, 020956, Bucharest, Romania
6 Poznan University of Medical Sciences, Faculty of Pharmacy, Industrial Pharmacy Division, Chair and Department of Pharmaceutical Technology, 60-806, Poznan, Poland

Download Full Article PDF

24. EFFICACY OF SALVIA MILTIORRHIZA EXTRACT INJECTION ON PERCUTANEOUS CORONARY INTERVENTION IN PATIENTS WITH CORONARY ATHEROSCLEROTIC HEART DISEASE

WEI LUO *, ZHAO XU, YI TANG

Department of Cardiology, Hunan Provincial People's Hospital (First Affiliated Hospital of Hunan Normal University), Changsha, 410016, Hunan, China

Download Full Article PDF

25. PHARMACIST INVOLVEMENT IN DIABETES MANAGEMENT

ANA-MARIA ATĂNĂSOIE, CRISTINA RAIS *, STANCU EMILIA, ADRIANA-

Department of Pharmaceutical Management and Marketing, Faculty of Pharmacy, "Carol Davila" University of Medicine and Pharmacy, 6 Traian Vuia Street, 020956, Bucharest, Romania

Download Full Article PDF

Home
Current Issue
Article Archive

Editorial Board
Scienti c Committee
History

Information for Authors
Subscriptions
Contact

FARMACIA - FARMACIAJOURNAL.COM

Farmacia

Romania | Universities and research institutions | Media Ranking

Country

SCIMAGO INSTITUTIONS RANKINGS

SCImago Media Rankings

Subject Area and Category

Pharmacology, Toxicology and Pharmaceutics

Pharmacology, Toxicology and Pharmaceutics (miscellaneous)

Publisher

Romanian Society for Pharmaceutical Sciences

SJR 2024

0.251

Q3

H-Index

33

Publication type

Journals

ISSN

00148237

Coverage

1945-1946, 1973-1987, 2003, 2008-2024

Information

Home

How to publish in this journal

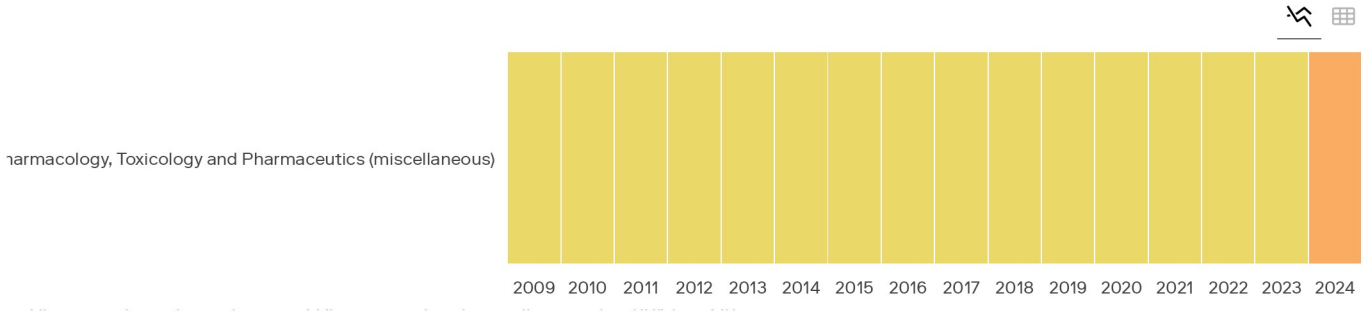
ssfr@revistafarmacia.ro

Scope

FARMACIA publishes original research papers, invited topical reviews and editorial commentaries and news, with emphasis on conceptual novelty and scientific quality. Main research areas are focused on: pharmacology, toxicology, medicinal chemistry, bio[illegible], dr[illegible], bi[illegible]

after the peer review precess. The papers should have not been published in any other journal. The recommendations of the Declaration of Helsinki, for humans, and the International guidelines as accepted principles for the use of experimental animals should be followed.

Quartiles



Find similar journals

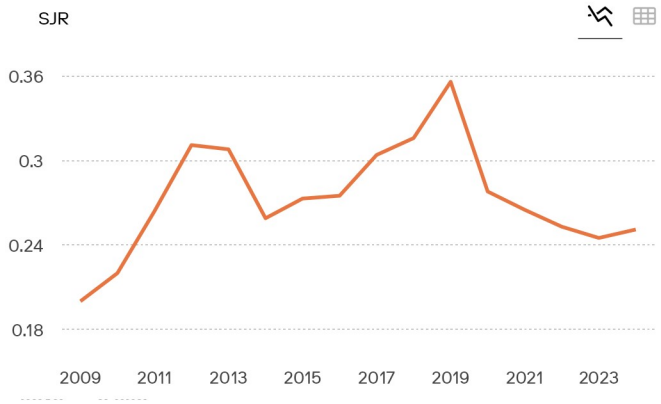
All quartiles All countries All subject categories Clear filters Download

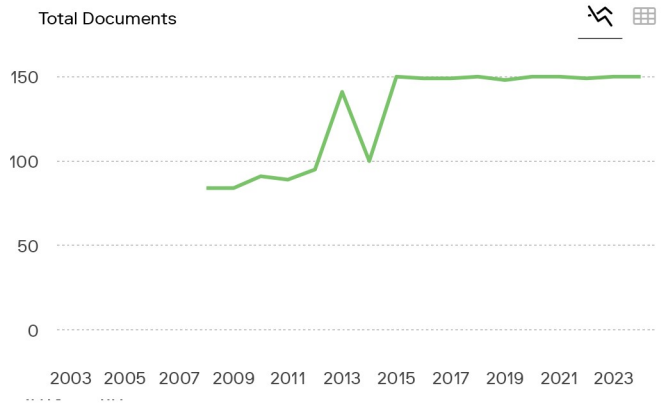
Only Open Access Journals

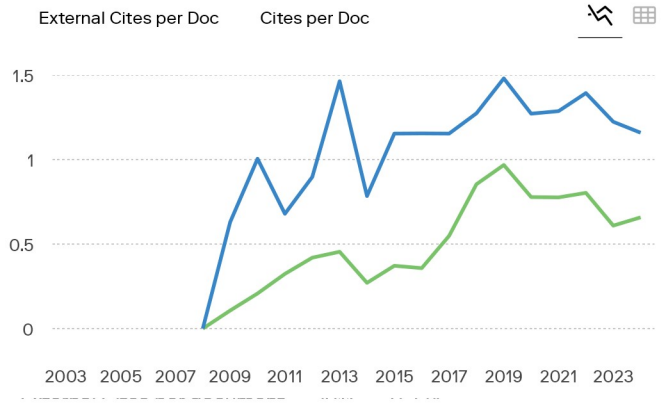
1 - Acta Poloniae Pharmaceutica - Drug Research
23%
similarity

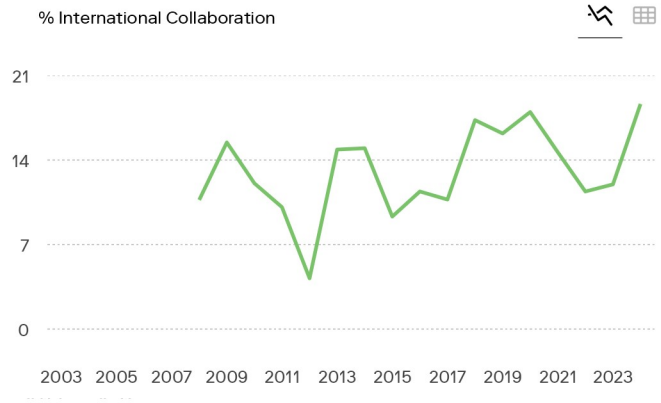
2 - Scientia Pharmaceutica
23%
similarity

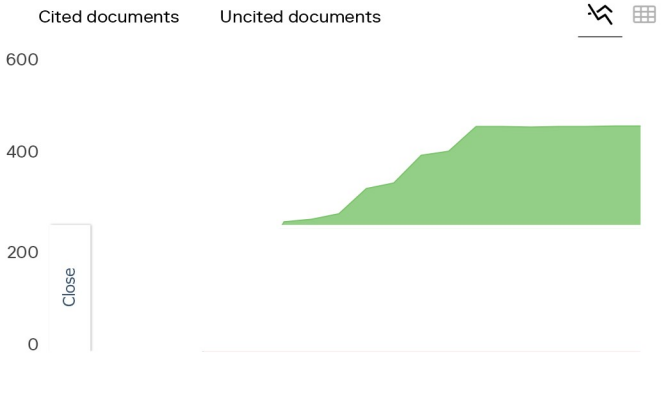
3 - Acta Pharmaceutica
22%
similarity

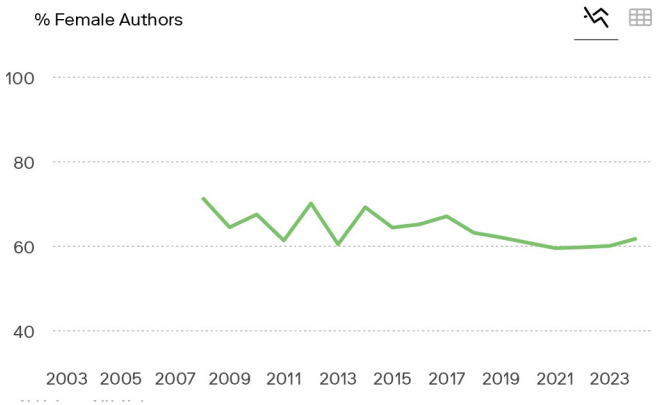


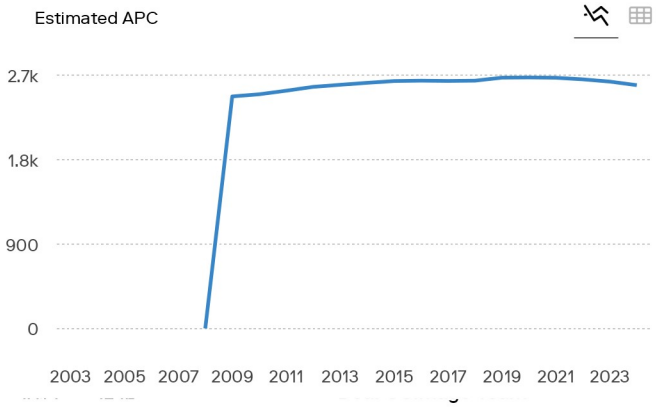


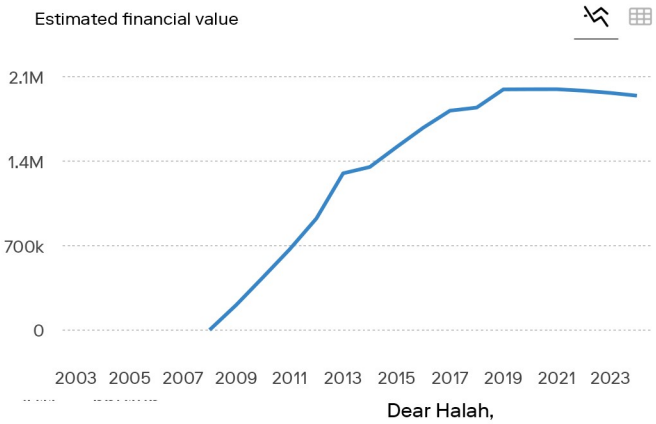






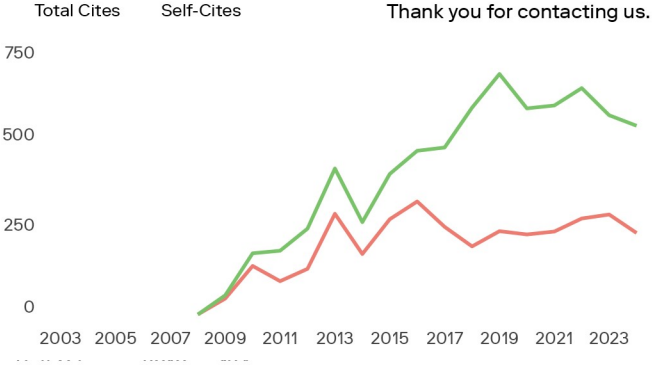






Dear Halah,

Thank you for contacting us.



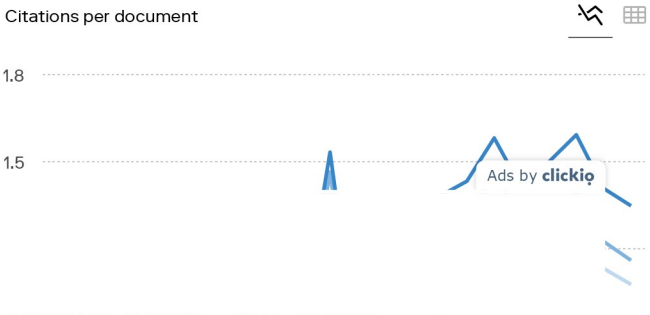
CImago Journal & Country Rank is not a journal. SJR
ndicators of journals indexed in Elsevier/Scopus.
al's homepage or contact the journal's editorial
u more deeply.

T **Tatev**

2 years ago

Dear colleague, can you specify the
not open?

reply

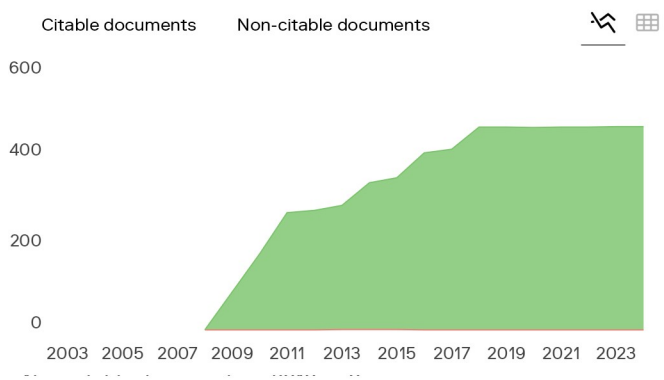


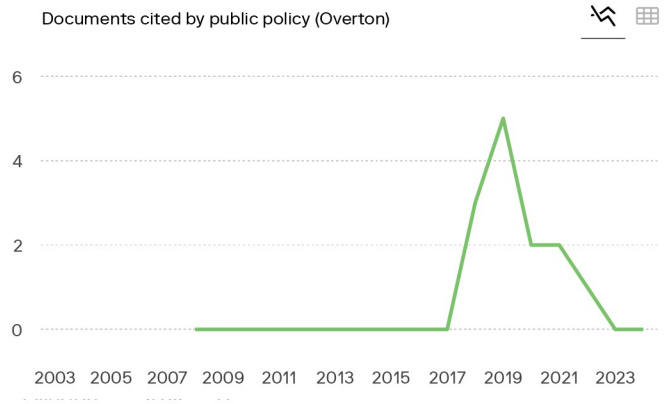
Close

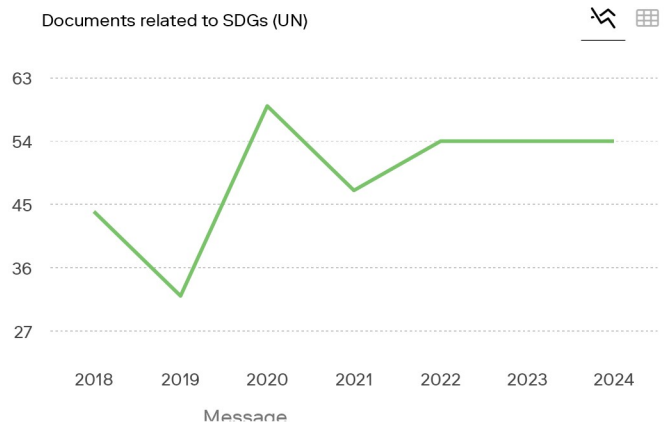
Melanie Ortiz
2 years ago

Dear Tatev, thank you very much for your comment. Unfortunately, we cannot help you with your request, we suggest you contact the journal's editorial staff so they could inform you more deeply. Best Regards, SCImago Team

G **gfriend**
6 years ago

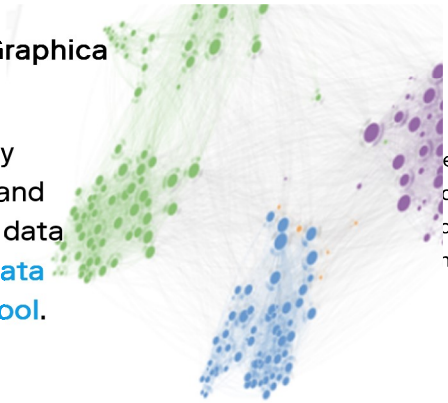






Show this widget in your own website

Just copy the code below and paste within your html



e possibility to dialogue through comments linked to a
ch general doubts about the processes of publication
om the publication of papers are resolved. For topics
ne usual channels with your editor.

Source details

Farmacia

Years currently covered by Scopus: from 1945 to 1946, from 1973 to 1987, 2003, from 2008 to 2025

Publisher: Romanian Society for Pharmaceutical Sciences

ISSN: 0014-8237

Subject area: Pharmacology, Toxicology and Pharmaceutics: General Pharmacology, Toxicology and Pharmaceutics

Source type: Journal

View all documents > | Set document alert | Save to source list

CiteScore 2024
2.2

SJR 2024
0.251

SNIP 2024
0.350

CiteScore | CiteScore rank & trend | Scopus content coverage

CiteScore 2024

$$2.2 = \frac{1.318 \text{ Citations } 2021 - 2024}{599 \text{ Documents } 2021 - 2024}$$

Calculated on 05 May, 2025

CiteScoreTracker 2025

$$2.2 = \frac{1.186 \text{ Citations to date}}{549 \text{ Documents to date}}$$

Last updated on 05 November, 2025 • Updated monthly

CiteScore rank 2024

Category	Rank	Percentile
Pharmacology, Toxicology and Pharmaceutics	#40/77	48th
General Pharmacology, Toxicology and Pharmaceutics		

View CiteScore methodology > | CiteScore FAQ > | Add CiteScore to your site

About Scopus

What is Scopus

Content coverage

Scopus blog

Scopus API

Privacy matters

Language

日本語版を表示する

查看简体中文版本

查看繁體中文版本

Просмотр версии на русском языке

Customer Service

Help

Tutorials

Contact us