

Phenothiazine und andere Dopaminantagonisten

„1876 wurden die beiden Farbstoffe Methylenblau und Thionin (Lauths Violett) hergestellt, die beide die Phenothiazin-Struktur enthalten. In den nächsten Jahren wurde Methylenblau als Mittel gegen Malaria, Kopfschmerzen oder Depressionen versucht, konnte sich jedoch nicht durchsetzen. ... In der Tiermedizin wurden sie als Wurmmittel eingesetzt.... Erst in den 1940er Jahren begann sich die medizinische Forschung wieder vermehrt den Phenothiazinen zuzuwenden. Die französische Pharmafirma Rhône-Poulenc entdeckte Phenothiazine mit antihistaminischen Eigenschaften. Dies führte 1950 zur Synthese von Neuroleptika (Chlorpromazin, Thorazine®)“. Quelle: <http://de.wikipedia.org/wiki/Phenothiazine>

Zellkerntherapeutika, cell nucleus therapeutics: Methylenblau (Rember®)

"In 1876, the two dyes methylene blue and thionine (Lauth's violet) were produced, both of which contain the phenothiazine structure. In the next few years, methylene blue has been used as an antimalarial drug, headache or depression but has failed. ... In veterinary medicine they were used as a worm remedy It was not until the 1940s that medical research began to turn increasingly to phenothiazines. The French pharmaceutical company Rhône-Poulenc discovered phenothiazines with antihistaminic properties. This led in 1950 to the synthesis of neuroleptics (chlorpromazine, Thorazine®) ".

“Phenothiazine is an organic compound that occurs in various antipsychotic and antihistaminic drugs. It has the formula $S(C_6H_4)_2NH$ The compound is related to the thiazine-class of heterocyclic compounds. Derivatives of the parent compound find wide use as drugs”. Source: <http://en.wikipedia.org/wiki/Phenothiazine>

Amaral L, Lorian V (1991) Effects of **chlorpromazine** on the cell envelope proteins of Escherichia coli. Antimicrob Agents Chemother 35, 9 1923-1924 Sep. [PMID](#)

Amaral L, Kristiansen J, Lorian V (1992) Synergic effect of **chlorpromazine** on the activity of some antibiotics. J Antimicrob Chemother 30, 4 556-558 Oct.

Amaral L, Kristiansen JE (2000) **Phenothiazines**: an alternative to conventional therapy for the initial management of suspected multidrug resistant tuberculosis. A call for studies. Int J Antimicrob Agents 14, 3 173-176 Apr.

Amaral L (2000) Management of intracellular infections with phenothiazines. Newsletter of the International Society of Chemotherapy. 3, 4

Amaral L, Kristiansen JE, Thomsen VF, Markovich B (2000) The effects of **chlorpromazine** on the outer cell wall of Salmonella typhimurium in ensuring resistance to the drug. Int J Antimicrob Agents 14, 3 225-229 Apr.

Amaral L, Kristiansen JE, Viveiros M, Atouguia J (2001) Activity of **phenothiazines against antibiotic-resistant Mycobacterium tuberculosis**: a review supporting further studies that may elucidate the potential use of thioridazine as anti-tuberculosis therapy. J Antimicrob Chemother 47, 5 505-511 May. [PMID](#)

L Amaral, J E Kristiansen (2001) **Phenothiazines: potential management of Creutzfeldt-Jacob disease and its variants**. Int J Antimicrob Agents 18, 5 411-417 Nov. [PMID](#)

Amaral L, Viveiros M, Kristiansen JE (2001) **Phenothiazines**: potential alternatives for the management of antibiotic resistant infections of tuberculosis and malaria in developing countries. Trop Med Int Health 6, 12 1016-1022 Dec. [PMID](#)

Ordway D, Viveiros M, Leandro C, Arroz MJ, Molnar J, Kristiansen JE, Amaral J (2002) **Chlorpromazine** has intracellular killing activity against phagocytosed Staphylococcus aureus at clinical concentrations. J Infect Chemother 8, 3 227-231 Sep. [DOI/PMID](#)

Ordway D, Viveiros M, Leandro C, Arroz MJ, Amaral L (2002) Intracellular activity of clinical concentrations of **phenothiazines including thioridazine** against phagocytosed Staphylococcus aureus. Int J Antimicrob Agents 20, 1 34-43 Jul. [PMID](#)

Grácio MA, dos Grácio AJ, Viveiros M, Amaral L (2003) Since **phenothiazines alter antibiotic susceptibility of microorganisms by inhibiting efflux pumps, are these agents useful for evaluating similar pumps in phenothiazine-sensitive parasites?** Int J Antimicrob Agents 22 3 347-351 Sep. [PMID](#)

Amaral L, Viveiros M, Molnar J (2004) Antimicrobial activity of **phenothiazines**. In Vivo 18, 6. 725-731 Nov/Dec. [PMID](#)

Hajos G, Riedl Z, Molnar J, Amaral L (2004) **NEW ACCESS TO PROMISING MDR INHIBITORY PHENOTHIAZINES** ANTICANCER RESEARCH 24, 3507-3508.

Pelegrini P, Franco OL (2005) **Plant Gamma-thionins: Novel insights on the mechanism of action of a multi-functional class of defense proteins.** The International Journal of Biochemistry & Cell Biology 37, 2239-2253 <https://www.ncbi.nlm.nih.gov/pubmed/16084753>
“**This last comparison offers some hypothesis for gamma-thionins mechanisms of action against certain pathogens. ... Finally, gamma-thionins activity has also been studied for future drug development, capable of inhibit tumor cell growth in human beings.**”

Amaral L, Martins M, Viveiros M (2007) **Phenothiazines** as anti-multi-drug resistant tubercular agents. Infect Disord Drug Targets 7, 3 257-265 Sep. [PMID](#)

[Ginimuge PR, Jyothi SD](#) (2010) **Methylene Blue: Revisited.** J Anaesthesiol Clin Pharmacol. 26(4), 517–520. PMID: PMC3087269 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3087269/?report=printab>
« **Methylene blue is used as a single dose of 1.5 -2 mg /kg IV over 20 min to 1hr for rescue treatment. ... Hence Methylene Blue is being investigated for the photodynamic treatment of cancer. ... The relationship between Methylene blue and Alzheimer's disease has recently attracted increasing scientific attention. It has been shown to attenuate the formations of amyloid plaques and neurofibrillary tangles and partial repair of impairments in mitochondrial function and cellular metabolism. ... Methylene blue is a safe drug when used in therapeutic doses (<2mg/kg). But it can cause toxicity in high doses. The features of toxicity being cardiac arrhythmias, coronary vasoconstriction, decreased cardiac output, renal blood flow and mesenteric blood flow; increased pulmonary vascular pressure & pulmonary vascular resistance and gas exchange deterioration. It also turns urine greenish blue and bluish discoloration of skin and mucosa which is self limiting. Due to its tissue reactive properties, a case of skin and fat necrosis followed by a dry gangrene of the skin in a female patient with breast cancer who underwent sentinel lymph node biopsy localization using peri-tumoral injection of Methylene blue dye has been reported. It can also cause hemolytic anemia characterized by Heinz body formation especially in pts with severe renal insufficiency and glucose-6-phosphate dehydrogenase (G6PD) deficiency. Neonates are particularly prone to adverse effects of Methylene blue. It causes hyperbilirubinemia, meth-Hemoglobin formation, hemolytic anemia, respiratory distress, pulmonary edema, photo toxicity and bluish discoloration of tracheal secretions and urine. Methylene Blue also interferes with the pulse oximeter's light emission resulting in falsely depressed oxygen saturation reading. Methylene blue due to its monoamine oxidase (MAO) inhibiting property may precipitate potentially fatal serotonin toxicity at doses >5mg/kg and rarely can cause severe anaphylactic shock.** »

Rodrigues L, Aínsa JA, Amaral L, Viveiros M (2011) **Inhibition of efflux pumps** of mycobacteria with **phenothiazines** and other putative efflux pump inhibitors (EPs) Patents Reviews Antinfective Drug Discovery 6 118-27 [DOI/PMID](#)

Varga ZG, Szabó MA, Schelz Z, Szeged Ei, Amaral L, Molnár J (2011) **Quorum Sensing Inhibition by Phenothiazines and Related Compounds** Letters in Drug Design & Discovery 8, 133-137 [DOI](#)

Jeyaseeli L, Dasgupta A, Dastidar SG, Molnar J, Amaral L (2012) **Evidences of Significant Synergism between Antibiotics and the Antipsychotic Antimicrobial Drug Flupenthixol** European Journal of Clinical Microbiology & Infectious Diseases 31, 6 1243-1250 Oct 14. [PMID](#)

Sachlos E, Risueno RM, Laronde S, Shapovalova Z, Lee JH, Russell J, Malig M, McNicol JD, Fiebig-Comyn A, Graham M, Levadoux-Martin M, Lee JB, Giacomelli AO, Hassell JA, Fischer-Russell D, Trus MR, et al. (2012) **Identification of drugs including a dopamine receptor antagonist that selectively target cancer stem cells**. Cell. 149(6),1284-1297.

Li J, Zhu S, Kozono D et al. (2014) Genome-wide shRNA screen revealed integrated mitogenic signaling between **dopamine receptor D2 (DRD2)** and epidermal growth factor receptor (EGFR) in **glioblastoma**. Oncotarget, [http://www.impactjournals.com/oncotarget/index.php?journal=oncotarget&page=article&op=view&path\[\]=1801&path\[\]=2156](http://www.impactjournals.com/oncotarget/index.php?journal=oncotarget&page=article&op=view&path[]=1801&path[]=2156)

Alassane D, Roh ME, Diawara H et al. (2018) **Efficacy and safety of primaquine and methylene blue for prevention of Plasmodium falciparum transmission in Mali: a phase 2, single-blind, randomised controlled trial**. The Lancet Infectious Diseases, DOI: [10.1016/S1473-3099\(18\)30044-6](https://doi.org/10.1016/S1473-3099(18)30044-6) [http://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(18\)30044-6/fulltext](http://www.thelancet.com/journals/laninf/article/PIIS1473-3099(18)30044-6/fulltext)

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