Ministry of Healthcare of Ukraine
National Pirogov Memorial Medical University

Germanyuk T.A., Bobruk V.P., Lysogora V.V.

GENERAL PHARMACOLOGY and PHARMACOLOGY of the drugs affecting mediatory processes, vegetative and central nervous systems

TUTORIAL

2015

UDC 615.2
LBC 52.81
G 39

Recommended by: the Central methodical Coordinating Council of National Pirogov Memorial Medical University as a Tutorial for the English- speaking students in higher pharmaceutical educational institutions of III-IV accreditation level of the specialty “Pharmacy” and “Clinical Pharmacy”. Approved, *Protocol № 5 from 18.03.2015.*

Reviewers:
Voloshchuk N.I. – doctor of medical sciences, Professor of pharmacology department of National Pirogov Memorial Medical University, Vinnytsya
Kryvoviaz O.V. – PhD, associate Professor, head of Pharmacy department of National Pirogov Memorial Medical University, Vinnytsya

G 39 **General Pharmacology and Pharmacology of the drugs affecting mediatory processes, vegetative and central nervous systems tutorial** / Germanyuk T.A., Bobruk V.P., Lysogora V.V. – Vinnytsya: Nilan-LTD, 2015 – 334P.

ISBN 978-966-924-096-5

The tutorial contains data concerning general conception of pharmacokinetics, pharmacodynamics, data about drugs affecting mediatory processes, vegetative nervous system, central nervous system, their classifications, lists of the drugs (International Nonproprietary Name, Proprietary commercial / brand / trade / generic names), medicinal forms, routs of administration and dose of the drugs, mechanisms of their action, pharmacological effects, including adverse effects and the ways to reduce them, indications, contraindications, the principles of rational combined use of the drugs, pharmacological drug safety and custody.

The tutorial is designed for students of higher pharmaceutical education institutions of III-IV level of accreditation in the specialty “Pharmacy” and “Clinical pharmacy”.

UDC 615.2
LBC 52.81

ISBN 978-966-924-096-5

Contents

Foreword

The tutorial "Pharmacology of the drugs affecting vegetative and central nervous system" includes the foundations of modern knowledge of the pharmacology of drugs that act on the peripheral and central nervous system (CNS) and is intended for students of a pharmacy department in specialty "Pharmacy" and "Clinical pharmacy".

Necessity to write a tutorial is caused by the need to provide the main aspects of current knowledge in pharmacology of drugs acting on the autonomic and central nervous system in accordance with the requirements of the credit-module system. According to the authors, the tutorial will be useful, given the fact of the necessity to intensify the efforts towards the students' independent work for the obtaining of knowledge in pharmacology.

The tutorial presents the key components of the pharmacokinetics and pharmacodynamics of the drugs with examples for better learning. In accordance with the tasks of pharmacology in this tutorial there are classifications of the drugs that affect the autonomic and central nervous system, according to the chemical structure, mechanisms of action, pharmacological effects; list of drugs (their INN and trade names, medicinal forms and routes of administration); mechanisms of action, pharmacological effects, including adverse effects, ways of reducing of the possible negative impact of a drug on the organism, indications and contraindications for use of the drugs, application features, pharmacological safety and pharmacological custody of the drugs, use of antidotes and symptomatic drugs in case of both, an overdose of drugs and the emergence of dangerous toxic effects.

The presented chapters of a tutorial show a close relationship of pharmacology with biology, normal and abnormal physiology, physics, normal and abnormal anatomy, biological chemistry, physical chemistry, pharmaceutical chemistry, etc. That is what allows correlating pharmacology with related medical sciences, to rethink the actions and uses of the drugs, to emphasize the applications of pharmacokinetics and pharmacodynamics to therapeutics to create the book that will be useful for the students of pharmacology, for the teachers of pharmacology and for the physicians.

The tutorial has a list of references, which were used by the authors and may be used by the students, teachers and physicians for improving personal knowledge in pharmacology.

The tutorial is written in accordance with the Program of pharmacology for the students of pharmaceutical faculty of higher educational institutions of III-IV accreditation levels for specialties 7.12020101 – "Pharmacy" and 7.12020102 – "Clinical Pharmacy" according to the educational qualification characteristics and educational and professional training program approved by the order of the Ministry of Healthcare of Ukraine dated 07.12.09 № 931 (period of study in this field – 5 years).

In today's pharmaceutical market there are so many drugs, which require a high level of knowledge of pharmacists and clinical pharmacists. The volume of

information about the mechanisms of drug action, their pharmacological effects, and the possibility of clinical use is growing rapidly. The position mentioned above leads to the necessity of teaching pharmacology to a much greater extent than it is provided in curriculum. Thence, the tutorial has been prepared based on the 5th release State Formulary of Ukraine in 2013, and the 66th issue of the British National Formulary of drugs in 2013, the 17th issue of the Russian Register of medicines in 2013, and the current literature on pharmacology and pharmacotherapy.

The authors of the tutorial are the teachers of the pharmacy department of Vinnitsa National Pirogov Memorial Medical University, Faculty of Pharmacy, with experience of teaching of pharmacology both in terms of previous training programs, and in terms of credit-modular system.

The authors are grateful to the reviewers who have put great efforts to improve the tutorial and gratefully accept all comments and suggestions from readers for further improvement of the tutorial.

List of abbreviations

AA - arachidonic acid
AANAT - arylalkylamine N-acetyltransferase
ACE - angiotensin-converted-enzyme
ACEI - angiotensin-converted-enzyme inhibitor
Ach - acetylcholine
AchE - acetylcholine esterase
ACTH - adreno-cortico-tropic hormone
ADME - absorption, distribution, metabolism, excretion of the drugs
ARs - adrenergic receptors
API - active pharmaceutical ingredient
ADP - adenosine diphosphate
ALX receptor(s) - lipoxin receptor(s)
AT receptor - angiotensin receptor
ATP - adenosine triphosphate
AV - block - atrio-ventricular blockage
AV- node - atrio-ventricular node
AVP - additional vasodilating propertie(s)
AUC - area under curve
Axe - acethylcholinesterase
BAS - biologically active substance(s)
BBB - blood brain barrier
BCSFB - blood-cerebrospinal fluid barrier
Ca^{+2} - calcium ion(s)
$C_{el.}$ - constant of elimination
cAMP - cyclic adenosine monophosphate
cGMP - cyclic guanosine monophosphate
Cl - total clearance
CNS - central nervous system
CO - carbon monoxide
COMT - catecol-orto-methyl-transferase
COX - cyclooxygenase
CysLT receptor(s) - cysteinyl leukotriene receptor(s)
D - dopamine
DAG - diacylglycerol
DNA - deoxyribonucleic acid
DDC - decarboxylase
DGLA - dihomo-γ-linolenic acid
EET - Epoxy-eicosa-trienoic acid
e.g. - for example
Ep - epinephrine
EPA - icosapentaenoic acid
E2 (PGE_2) - prostaglandin E2

F2α ($PGF_{2\alpha}$) - prostaglandin F2α
FDA - Food and Drug Administration
FFA - free fatty acid
fMLP - Formyl-Methionyl-Leucyl-Phenylalanine
GIT - gastrointestinal tract
GPCR - G-protein-coupled receptor(s)
H_2S - hydrogen sulphide
h/chl. - hydrochloride
h/tr. - hydrotartrat
I2 (PGI_2) - prostacyclin
i.e. - that is
IHD - ischemic heart disease
i/m - intramuscularly
INN - international nonproprietary name
IP_3 - inositol 1,4,5-trisphosphate
ISA - intrinsic sympathomimetic activity
i/v - intravenous
$K_{el.}$ - constant of elimination
LTs - leucotriens
LXA4- lipoxin A4
MAO - monoaminoxydase
MAOI - MAO inhibitor
MIC - minimum inhibitory concentration
MF - medicinal form
MP - medicinal preparation
NE - norepinephrine
NO - nitric oxide
OTC - over-the-counter
P receptor(s) - purine receptor(s)
PAE - “postantibiotic” effect
PAF - platelet-activating factor
PB - placental barrier
PGs - prostaglandins
PI - phosphatidylinositol
PLA2 - phospholipase A2
PLC - phospholipase C
RNA - ribonucleic acid
s/c - subcutaneously
Se - serotonine
SNRI(s) - serotonine-norepinephrine reuptake inhibitor(s)
SSRI(s) - selective serotonine reuptake inhibitor(s)
SVT - supraventricular tachycardia
TCA(s) - tricyclic antidepressant(s)
TG - triglyceride(s)

TI - Therapeutic index
TPH - tryptophan hydroxylase
Tx - thromboxane
TxA_2 - thromboxane A2
$T_{1/2}$ - half-life
V - volume distribution
USAN - United States Adopted Name(s)
WHO - World Health Organization
WPW syndrome - Wolff-Parkinson-White syndrome
5-HIAA - 5-hydroxyindoleacetic acid
5-HT - 5-hydroxytryptamine
5-LOX - 5-lipoxigenase

Introduction

Pharmacology is the study of the interactions that occur between medical devices, biologically active substances with a living organism. **Pharmacology** is concerned with the study of medical devices, which are used for treatment, prevention and diagnostics of diseases and pathological conditions. From Greek "**pharmacon**" – there is drug and "**logos**" – there is a science. **Pharmacology** is the branch of medicine which is connected with other disciplines such as biology, chemistry, normal and pathological anatomy, normal and pathological physiology, histology and pharmaceutical sciences such as pharmaceutical chemistry and toxic chemistry, pharmacognosy and drug technology.

To the sciences about drugs belongs not only pharmacology but also pharmacy. And if pharmacology is a science that deals with the effect and usage of medicines, so **pharmacy** is a science that deals with the preparation and dispensing of drugs.

An active pharmaceutical ingredient (medical substance (MS) or active substance) (API) – is any substance or mix of substances that is used in manufacture of drugs and during its usage exerts pharmacological activity. Such substances have pharmacological or other direct effect on the human body; in the composition of the prepared forms of drugs which are used for cure, diagnosis and prevention of diseases, for the change of condition, structures or physiological functions of the organism, for care, treatment and facilitation of symptoms. (The order of The Ministry of Health of Ukraine № 723, completed in accordance with The Ministry of Health of Ukraine № 427 (z0923-13) dated 24.05.2013).

Pharmaceutical drug – is any substance or combination of substances (one or more API and excipients) that has properties and is intended for use in the treatment or prevention of diseases or it's any substance or combination of substances (one or more API and excipients) that can be prescribed for the pregnancy prevention, restoration, correction or change of physiological functions in humans by providing pharmacological, immunological or metabolic actions, or for diagnosis.

Medicinal Form (MF) – is a combination of the form in which a drug is submitted by the manufacturer (release form), and also the forms in which a drug is prescribed for usage including physical form (the form of usage).

Medicinal preparation (MP) – is a drug that is made in the appropriate dosage (medicinal) form. Medical preparations can be simple which are made from medical raw material (usually from plants, but also can be of mineral and animal origin) using a simple processing (drying or grinding), complex or galenicals, which are made by using more complex processing of plant raw materials with extraction (by alcohol, ether, water) of biologically active components and their partial exemption from impurities (ballast substances). These are tinctures and extracts. However galenicals contain many impurities (proteins, coloring substances, mucuses, etc.) which reduce the effect of the preparation, may cause a pharmacological effect which differs from that of the purified substance (e.g., there

is no equality between the pharmacological effect of opium galenic preparations and morphine, between the extract of uterine horn and ergometrine, between the ascorbic acid and rosehip extract, etc.) and do not allow its parenteral use. Neogalenicals are made by the pharmaceutical industry. They are more purified of ballast substances, have a longer expiration date, less of side effects and are suitable for parenteral use. (e.g., atropine, platyphylline, morphine, ephedrine, digoxin, strophanthin etc.). Each MP is registered in the state register of the pharmaceutical drugs of the country.

Some drugs are in an inactive form and in order to convert them into an active form, they should be metabolized in the human body and should form metabolites that have pharmacological activity. These drugs are called prodrugs.

Substances with medicinal properties can be synthesized within the human body (e.g., hormones) or may be xenogenic to the human body, the so-called xenobiotics *(Greek xenos – "alien ")*.

Some drugs are administered as racemic mixtures of stereoisomers. The stereoisomers can exhibit different pharmacodynamic as well as pharmacokinetic properties. More than half of the drugs exist as enantiomeric pairs: *R (+)* enantiomeric, *S (-)* enantiomeric and the racemic mixture *RS (+ / -)*.

Drugs have three main names:

1) *the chemical name*, which reflects the chemical structure of drugs and is rarely used in medical practice, but often – in the annotations to the drugs and in the reference books. For example, 2-acetoxy-benzoic acid (acid acetylsalicylic).

2) *international nonproprietary name (INN) of drugs*. This name of drugs is offered by the WHO (World Health Organization) and is adapted for use worldwide in the academic and scientific literature for easier identification by experts and for prevention of errors in determining generic / trade names of drugs. *For example*, acid acetylsalicylic (2-acetoxy-benzoic acid).

3) commercial / trade name (brand names) is given by pharmaceutical companies / manufacturers of drugs and is a commercial property, protected by patents and indicated by a pictogram – an English letter "R" inside a circle. *For example*, Aspirin ® (2 -acetoxy-benzoic acid, acid acetylsalicylic). Trade name is used by the company that produces these drugs for marketing purposes, to advance it in the market and to compete with other similar drugs. After the expiration of the patent the manufacturer can sell the right to produce drugs under the INN. Such drugs are called generics (branded equivalent). Generics are usually cheaper than original drugs because their price does not include money spent on development, preclinical and clinical drug testing. *For example*, Trombo ASS (2-acetoxy-benzoic acid, acid acetylsalicylic, Aspirin).

Equal drug substances may contain the same doses of a chemical substance in one dosage form and have different trade names (synonyms). Thus, the pharmacist can make a so-called generic substitution of drugs, focusing on its INN, in the absence of drugs recommended by your doctor or the drugs required by the patient in the drugstore. *For example*, (2-acetoxy-benzoic acid, acid acetylsalicylic, Aspirin, Trombo ASS).

Peculiarities of marking of ready dosage forms

The symbol «®» *(from English "Registered trademark" – the registered mark)* is a marking which is written down on the package near a certain brand name and means the registration of the mark as a trademark for goods. In the registration certificate and other registration documents the symbol «®» is written down next to the trade name of medicinal preparation.

Tablets with a modified release are covered or uncovered tablets which contain special excipients or substances received by a special technology that allow to program the speed or location of the release of the medical substance (the modified-release tablets – MR). The name is used to mark the tablets with a controlled release, sustained-release (SR) tablets, and tablets with a gradual release, prolonged/extended release (ER). The name is not used to name the tablets that are indicated as the depot tablets, tablets that are implanted, retard-tablets, rapid-retard tablets.

There are **Drug Delivery Systems**: *Osmotic Release Oral System (OROS)* – there is the system based on the principle of osmotic pump, with which there is a constant controlled release of a drug in a unit time; *Transdermal System (TS)* of drug delivery in the form of patches; *Gastrointestinal Therapeutic System (GITS)*, which provide release of drug substances from the medicinal forms in a neutral, acidic or alkaline environment of gastrointestinal tract GIT; *Orally disintegrating tablet (ODT)*, *dry powder inhalers (DPI)*, *metered-dose inhalers (MDI)*, etc. The main merit of therapeutic systems is improvement in bioavailability as well as reduced adverse effects and limitation of high initial drug concentrations in plasma and opportunity to change the mode of taking drugs, dosing regimen on a convenient for the patients.

Retard tablets are tablets with a prolonged (periodic) release of medical substance from the stock. Usually they are in the shape of microgranules from a medical substance, surrounded by a biopolymer matrix (base), a base or microgranules are dissolve in layers releasing another portion of medical substance.

Rapid tablets contain a mixture of microgranules with an immediate release of medical substance.

Rapid retard tablets are tablets with a biphasic release that contain a mixture of microgranules with a rapid and prolonged release of the medical substance.

Tablets UNO – a recommended average dose for adults and children over 12 years is 1 tablet every 24 hours.

The tablets durules provide a gradual release of the active ingredient (iron ions) during a long time. The plastic matrix of the tablets Sorbifer Durules is completely inert in the digestive juice, but is completely dissolved under the influence of the intestinal peristalsis, when the active ingredient is completely released.

There are **international standards (International rules-standards)**, which determine the process of production of drugs: **GMP** – good manufactory practice; **GLP** – good laboratory practice – appropriate preclinical drug testing: on animals, test-systems (ex vivo), on cells, etc.; **GCP** – good clinical practice – appropriate clinical drug testing: on healthy volunteers, on patients; **GDP** – good distribution practice – appropriate practice of distribution of drugs; **GPP** – good pharmacy practice.

Despite the complexity of the creation and production of new drugs and their generics, new dosage forms, the study and specification of the action mechanisms in accordance with new knowledge in related sciences, the discovery of new pharmacological effects of the known drugs, determination of pharmacological safety, pharmacological custody and the combined use of medicine, pharmacology and pharmacy are very fast-developing sciences that require a constant monitoring and addition in teaching in the learning process.

Pharmacology includes **Pharmacokinetics** and **Pharmacodynamics.**

In order to understand and control drug action in the human body, one needs to know how a drug reaches the site(s) of drug action and when this will happen. Besides, understanding biochemical and physiological effects of the drugs and their mechanisms of action can provide the basic for the rational therapeutic use of the drugs and development of new and better therapeutic agents. More over, the adverse effects of the drugs and their toxicity can be expected by understanding a drug's mechanism(s) of action, its pharmacokinetics, and its interactions with other drugs. Thereby, both the pharmacodynamic properties of a drug and its pharmacokinetics promote the safe and successful therapy. It is necessary to remember that the effects of many drugs, both curative and maleficent, may differ widely from patient to patient due to genetic differences that alter pharmacokinetic and pharmacodynamic of a given drug.

REFERENCES

1. A Roadmap to Key Pharmacologic Principles in Using Antipsychotics. Prim Care Companion J Clin Psychiatry 9 (6): 444-54. (June 2007)
2. ADRAC (2004). "Cardiac valvulopathy with pergolide". *Aust Adv Drug React Bull* **23** (4). Free full text from the Australian Therapeutic Goods Administration.
3. Alvarez, EO (2009). "The role of histamine on cognition.". *Behavioural Brain Research* **199** (2): 183–9.
4. Alvarez, R., Taylor, A., Fazzari, J. J. and Jacobs, J. R. (1981) Regulation of cyclic AMP metabolism in human platelets. Sequential activation of adenylate cyclase and cyclic AMP phosphodiesterase by prostaglandins. *Mol. Pharmacol.*, **20**: 302-309.
5. Arias-Carrión O, Pöppel E (2007). "Dopamine, learning and reward-seeking behavior". *Act Neurobiol Exp* **67** (4): 481–488.
6. Bartsch, T., Knight, Y. E. and Goadsby, P. J. (2004) Activation of 5-HT(1B/1D) receptor in the periaqueductal gray inhibits nociception. *Ann Neurol*, **56**: 371-381.
7. Ben-Jonathan N, Hnasko R (2001). "Dopamine as a Prolactin (PRL) Inhibitor" (PDF). *Endocrine Reviews* 22 (6): 724–763.
8. Benneyworth MA, Xiang Z, Smith RL, Garcia EE, Conn PJ, Sanders-Bush E (August 2007). "A selective positive allosteric modulator of metabotropic glutamate receptor subtype 2 blocks a hallucinogenic drug model of psychosis". *Molecular Pharmacology* **72** (2): 477–84.
9. Berger M, Gray JA, Roth BL (2009). "The expanded biology of serotonin". *Annu. Rev. Med.* **60**: 355–66.
10. Bertil B. Fredholm, Adriaan P. Ijzerman, Bruno G. Frenguelli, Rebecca Hills, Kenneth A. Jacobson, Joel Linden, Ulrich Schwabe, Gary L. Stiles. Adenosine receptors. Last modified on 17/02/2012. Accessed on 10/06/2012. IUPHAR database (IUPHAR-DB). http://www.iuphar-db.org/DATABASE
11. Bertram G. Katzung. Basic & Clinical Pharmacology. Lange Medical Books/McGraw-Hill. Medical Published Division. 2003. – 1202p.
12. Bieri, Stefan; Anne Brachet, Jean-Luc Veuthey, Philippe Christen (2006). «Cocaine distribution in wild Erythroxylum species». Journal of Ethnopharmacology **103** (3): 439-447.
13. Bockaert, J., Claeysen, S., Compan, V. and Dumuis, A. (2004) 5-HT4 receptors. *Curr Drug Targets CNS Neurol Disord.*, **3**: 39-51.

14. Bockaert, J; Claeysen, S; Bécamel, C; Dumuis, A; Marin, P. (2006) Neuronal 5-HT metabotropic receptors: fine-tuning of their structure, signaling, and roles in synaptic modulation. *Cell Tissue Res.*, **326** (2): 553-72.
15. Boyer EW, Shannon M (March 2005). «The serotonin syndrome». N. Engl. J. Med. ***352** (11): 1112–20.*
16. Brenchat, A; Romero, L; García, M; Pujol, M; Burgueño, J; Torrens, A; Hamon, M; Baeyens, JM; Buschmann, H; Zamanillo, D; *et al.*. (2009) 5-HT7 receptor activation inhibits mechanical hypersensitivity secondary to capsaicin sensitization in mice. *Pain*, **141** (3): 239-47.
17. British National Formular. https://www.bnf.org
18. Browman, KE; Curzon, P; Pan, JB; Molesky, AL; Komater, VA; Decker, MW; Brioni, JD; Moreland, RB et al. (2005). "A-412997, a selective dopamine D4 agonist, improves cognitive performance in rats". *Pharmacology, Biochemistry, and Behavior* **82** (1): 148–55.
19. Brown RA, Spina D, Page CP (March 2008). "Adenosine receptors and asthma". *Br. J. Pharmacol.* 153 Suppl 1 (S1): S446–56.
20. Buckland, K. F., Williams, T. J. and Conroy, D. M. (2003) Histamine induces cytoskeletal changes in human eosinophils via the H(4) receptor. *Br J Pharmacol*, **140**: 1117-1127.
21. Cannon, K. E., Nalwalk, J. W., Stadel, R., Ge, P., Lawson, D., Silos-Santiago, I. and Hough, L. B. (2003) Activation of spinal histamine H3 receptors inhibits mechanical nociception. *Eur J Pharmacol*, **470**: 139-147.
22. Cará, AM; Lopes-Martins, RA; Antunes, E; Nahoum, CR; De Nucci, G (1995). "The role of histamine in human penile erection.". *British journal of urology* **75** (2): 220–4.
23. Cervenka, S; Pålhagen, SE; Comley, RA; Panagiotidis, G; Cselényi, Z; Matthews, JC; Lai, RY; Halldin, C et al. (2006). "Support for dopaminergic hypoactivity in restless legs syndrome: a PET study on D2-receptor binding". *Brain* **129** (Pt 8): 2017–28.
24. Chekman I., Gorchakova N., Panassenko N., Bekh P. Pharmacology. VINNYTSYA. 2006. – 382p.
25. Cogé, F., Guénin, S. P., Audinot, V., Renouard-Try, A., Beauverger, P., Macia, C., Ouvry, C., Nagel, N., Rique, H., Boutin, J. A. and Galizzi, J. P. (2001) Genomic organization and characterization of splice variants of the human histamine H3 receptor. *Biochem J*, **355**: 279-288.
26. Coleman, R. A., Kennedy, I., Humphrey, P. P. A., Bunce, K. and Lumley, P. (1990) Prostanoids and their receptors. *in* Comprehensive Medicinal

Chemistry *Edited by* Hansch, C. Sammes, P. G. and Taylor, J. B. Pergamon Press. 643-714

27. Coleman, R. A., Smith, W. L. and Narumiya, S. (1994) VIII. International Union of Pharmacology classification of prostanoid receptors: properties, distribution and structure of the receptors and their subtypes. *Pharmacol. Rev.*, **46**: 205-229.
28. Consumer Health Resource Group, LLC (2009-09-19). "Abilify Side Effects". www.askapatient.com. Retrieved 2009-09-29.
29. Corbett AD, Henderson G, McKnight AT, Paterson SJ (2006). «75 years of opioid research: the exciting but vain quest for the Holy Grail». Br. J. Pharmacol. 147 Suppl 1: S153–62.
30. Crawford, M., Ford, S., Henry, M., Matherne, G. P. and Lankford, A. (2005) Myocardial function following cold ischemic storage is improved by cardiac-specific overexpression of A1-adenosine receptors. *Can J Physiol Pharmacol*, **83**: 493-498.
31. Davidson S, Prokonov D, Taler M, Maayan R, Harell D, Gil-Ad I, Weizman A (2009). "Effect of exposure to selective serotonin reuptake inhibitors in utero on fetal growth: potential role for the IGF-I and HPA axes". *Pediatr. Res.* **65** (2): 236–41.
32. Deng, C; Weston-Green K; Huang XF (1 February 2010). "The role of histaminergic H1 and H3 receptors in food intake: A mechanism for atypical antipsychotic-induced weight gain?". *Progress in Neuro-Psychopharmacology and Biological Psychiatry* **34** (1): 1–4.
33. Di Giuseppe, M., et al. (2003). *Nelson Biology 12*. Toronto: Thomson Canada Ltd.. p. 473.
34. Drogovoz S.M. PHARMACOLOGY. CITO. Kharkiv. 2009. – 230p.
35. Drogovoz S.M., Kutsenko T.A. PHARMACOLOGY at your palms. Kharkiv. 2010. – 77p.
36. Dubey, R. K., Gillespie, D. G., Mi, Z. and Jackson, E. K. (2005) Adenosine inhibits PDGF-induced growth of human glomerular mesangial cells via A(2B) receptors. *Hypertension*, **46**: 628-634.
37. Dunkley EJ, Isbister GK, Sibbritt D, Dawson AH, Whyte IM (2003). "The Hunter Serotonin Toxicity Criteria: simple and accurate diagnostic decision rules for serotonin toxicity". *QJM* **96** (9): 635–42.
38. Egashira N, Ishigami N, Pu F et al. L-Theanine relieves positive, activation, and anxiety symptoms in patients with schizophrenia and schizoaffective disorder: an 8-week, randomized, double-blind, placebo-controlled, 2-center study, J Clin Psychiatry 2010;71:1-9 (2 September 2007).

39. Falzone, T. L., Gelman, D. M., Young, J. I., Grandy, D. K., Low, M. J. and Rubinstein, M. (2002) Absence of dopamine D4 receptors results in enhanced reactivity to unconditioned, but not conditioned, fear. *Eur J Neurosci*, **15**: 158-164.
40. Fell MJ, Svensson KA, Johnson BG, Schoepp DD (July 2008). "Evidence for the role of metabotropic glutamate (mGlu)2 not mGlu3 receptors in the preclinical antipsychotic pharmacology of the mGlu2/3 receptor agonist (-)-(1R,4S,5S,6S)-4-amino-2-sulfonylbicyclo[3.1.0]hexane-4,6-dicarboxylic acid (LY404039)". *The Journal of Pharmacology and Experimental Therapeutics* **326** (1): 209–17.
41. Fine Perry G. Chapter 2: The Endogenous Opioid System // A Clinical Guide to Opioid Analgesia. — McGraw Hill, 2004.
42. Food and Drug Administration Public Health Advisory". 2007-03-29. Retrieved 2010-02-07.
43. Fredholm, BB; IJzerman, AP; Jacobson, KA; Klotz, KN; Linden, J. (2001) International Union of Pharmacology. XXV. Nomenclature and classification of adenosine receptors. *Pharmacol. Rev.*, **53** (4): 527-52.
44. Frost M, Andersen T, Gossiel F, Hansen S, Bollerslev J, Van Hul W, Eastell R, Kassem M, Brixen K. (2011). "Levels of serotonin, sclerostin, bone turnover markers as well as bone density and microarchitecture in patients with high bone mass phenotype due to a mutation in Lrp5". *J Bone Miner Res.* **26** (8): 1721–8.
45. Fujii H, Nagase H (2006). «Rational drug design of selective epsilon opioid receptor agonist TAN-821 and antagonist TAN-1014». Curr. Med. Chem. 13 (10): 1109–18.
46. Fujii H, Narita M, Mizoguchi H, Murachi M, Tanaka T, Kawai K, Tseng LF, Nagase H (August 2004). «Drug design and synthesis of epsilon opioid receptor agonist: 17-(cyclopropylmethyl)-4,5alpha-epoxy-3,6beta-dihydroxy-6,14-endoethenomorphinan-7alpha-(N-methyl-N-phenethyl)carboxamide (TAN-821) inducing antinociception mediated by putative epsilon opioid receptor». *Bioorg. Med. Chem.* 12 (15): 4133–45.
47. Gansij T.V. STUDY GUIDE to BASIC PHARMACOLOGY. Kharkiv. 2005. – 260p.
48. Gildea, John J (2009). "Dopamine and angiotensin as renal counterregulatory systems controlling sodium balance". *Current Opinion in Nephrology and Hypertension* **18** (1): 28–32.
49. Giles, H., Leff, P., Bolofo, M. L., Kelly, M. G. and Robertson, A. D. (1989) The classification of prostaglandin DP-receptors in platelets and vasculature

using BW A868C, a novel, selective, and potent competitive antagonist. *Br. J. Pharmacol.*, **96**: 291-300.

50. Goldberg L., Kohli J. (1983). «Peripheral dopamine receptors: a classification based on potency series and specific antagonism». *Trends Pharm. Sci.* **4**: 64.
51. Gonzalez, R., Echeverria, E., Reinicke, K. and Rudolph, M. I. (1994) Increased affinity of histamine H1 binding to membranes of human myometrium at the end of pregnancy. *Gen Pharmacol*, **25**: 1607-1610.
52. González-Maeso J, Ang RL, Yuen T et al. (March 2008). "Identification of a Novel Serotonin/Glutamate Receptor Complex Implicated in Psychosis". *Nature* **452** (7183): 93–7.
53. Goodman & Gilman's The Pharmacological Bases of THERAPEUTICS. 12 edition. Medical. 2011. – 2084 P.
54. Grattan, D. R., Steyn, F. J., Kokay, I. C., Anderson, G. M. and Bunn, S. J. (2008) Pregnancy-induced adaptation in the neuroendocrine control of prolactin secretion. *J Neuroendocrinol*, **20**: 497-507.
55. Hardie RC (June 1989). "A histamine-activated chloride channel involved in neurotransmission at a photoreceptor synapse". *Nature* **339** (6227): 704–6.
56. Hayaishi, O., Matsumura, H., Onoe, H., Koyama, Y. and Watanabe, Y. (1991) Sleep-wake regulation by PGD_2 and E_2. *Adv. Prostaglandin Thromboxane Leukotriene Res.*, **21**: 723-726.
57. Heijtz RD, Kolb B, Forssberg H (2007). "Motor inhibitory role of dopamine D1 receptors: implications for ADHD" (PDF). *Physiol Behav* 92 (1–2): 155–160.
58. Heusler, P; Palmier, C; Tardif, S; Bernois, S; Colpaert, FC; Cussac, D. (2010) [(3)H]-F13640, a novel, selective and high-efficacy serotonin 5-HT(1A) receptor agonist radioligand.
59. Hirai, H., Abe, H., Tanaka, K., Takatsu, K., Sugamura, K., Nakamura, M. and Nagata, K. (2003) Gene structure and functional properties of mouse CRTH2, a prostaglandin D2 receptor. *Biochem Biophys Res Commun*, **307**: 797-802.
60. Hirai, H., Tanaka, K., Takano, S., Ichimasa, M., Nakamura, M. and Nagata, K. (2002) Cutting edge: agonistic effect of indomethacin on a prostaglandin D2 receptor, CRTH2. *J Immunol*, **168**: 981-985.
61. Holenz, J; Mercè, R; Díaz, JL; Guitart, X; Codony, X; Dordal, A; Romero, G; Torrens, A; Mas, J; Andaluz, B; *et al.*. (2005) Medicinal chemistry driven approaches toward novel and selective serotonin 5-HT6 receptor ligands. *J. Med. Chem.*, **48** (6): 1781-95.

62. http://astrobiology.berkeley.edu/PDFs_articles/WineAnalysisAnalChem.pdf
63. Huang, Y. Y., Oquendo, M. A., Friedman, J. M., Greenhill, L. L., Brodsky, B., Malone, K. M., Khait, V. and Mann, J. J. (2003) Substance abuse disorder and major depression are associated with the human 5-HT1B receptor gene (HTR1B) G861C polymorphism. *Neuropsychopharmacology*, **28**: 163-169.
64. Hyun, J. S., Baig, M. R., Yang, D. Y., Leungwattanakij, S., Kim, K. D., Abdel-Mageed, A. B., Bivalacqua, T. J. and Hellstrom, W. J. (2002) Localization of peripheral dopamine D1 and D2 receptors in rat and human seminal vesicles. *J Androl*, 23: 114-120.
65. Isbister, G. K.; Bowe, S. J.; Dawson, A.; Whyte, I. M. (2004). "Relative toxicity of selective serotonin reuptake inhibitors (SSRIs) in overdose". *J. Toxicol. Clin. Toxicol.* **42** (3): 277–85.
66. Isbister, G. K.; Bowe, S. J.; Dawson, A.; Whyte, I. M. (2004). «Relative toxicity of selective serotonin reuptake inhibitors (SSRIs) in overdose». J. Toxicol. Clin. Toxicol. **42** (3): 277–85.
67. Ito, C (2004). "The role of the central histaminergic system on schizophrenia". *Drug news & perspectives* **17** (6): 383–7.
68. Ito, S., Negishi, M., Sugama, K., Okuda-Ashitaka, K. and Hayaishi, O. (1990) Signal transduction coupled to prostaglandin D_2. *Adv. Prostaglandin Thromboxane Leukotriene Res.*, **21**: 371.
69. IUPHAR DATABASE. International Union of Basic and Clinical Pharmacology 2012. http://www.iuphar-db.org/DATABASE/
70. Jääskeläinen, SK; Rinne, JO; Forssell, H; Tenovuo, O; Kaasinen, V; Sonninen, P; Bergman, J. (2001). "Role of the dopaminergic system in chronic pain -- a fluorodopa-PET study". *Pain* **90** (3): 257–60.
71. Jähnichen S, Horowski R, Pertz H. "Pergolide and Cabergoline But not Lisuride Exhibit Agonist Efficacy at Serotonin 5-HT2B Receptors". Retrieved 2010-02-03.
72. Jansen-Olesen, I., Ottosson, A., Cantera, L., Strunk, S., Lassen, L. H., Olesen, J., Mortensen, A., Engel, U. and Edvinsson, L. (1997) Role of endothelium and nitric oxide in histamine-induced responses in human cranial arteries and detection of mRNA encoding H1- and H2-receptors by RT-PCR. *Br J Pharmacol*, **121**: 41-48.
73. Jiang, M., Spicher, K., Boulay, G., Wang, Y. and Birnbaumer, L. (2001) Most central nervous system D2 dopamine receptors are coupled to their effectors by Go. *Proc Natl Acad Sci U S A*, **98**: 3577-3582.

74. Johnson DJ, Sanderson H, Brain RA, Wilson CJ, Solomon KR (2007). "Toxicity and hazard of selective serotonin reuptake inhibitor antidepressants fluoxetine, fluvoxamine, and sertraline to algae". *Ecotoxicol. Environ. Saf.* **67** (1): 128–39.
75. Kang K, Park S, Kim YS, Lee S, Back K (2009). "Biosynthesis and biotechnological production of serotonin derivatives". *Appl. Microbiol. Biotechnol.* **83** (1): 27–34.
76. Kars, M., Pereira, A. M., Bax, J. J. and Romijn, J. A. (2008) Cabergoline and cardiac valve disease in prolactinoma patients: additional studies during long-term treatment are required. *Eur J Endocrinol*, **159**: 363-367.
77. Kars, M., Pereira, A. M., Bax, J. J. and Romijn, J. A. (2008) Cabergoline and cardiac valve disease in prolactinoma patients: additional studies during long-term treatment are required. *Eur J Endocrinol*, **159**: 363-367.
78. Katoh, H., Watabe, A., Sugimoto, Y., Ichikawa, A. and Negishi, M. (1995) Characterization of the signal transduction of prostaglandin E receptor EP_1 subtype in cDNA-transfected Chinese hamster ovary cells. Biochim. Biophys. *Acta*, 1244: 41-48.
79. Katzung, Trevor et al. Pharmacology Board Review. p.153. Mcgraw Hill, 2007.
80. Kemp, A. and Manahan-Vaughan, D. (2005) The 5-hydroxytryptamine4 receptor exhibits frequency-dependent properties in synaptic plasticity and behavioural metaplasticity in the hippocampal CA1 region in vivo. *Cereb Cortex*, **15**: 1037-1043.
81. King MW. "Serotonin". *The Medical Biochemistry Page*. Indiana University School of Medicine. Retrieved 2009-12-01.
82. Kita, J. M., Parker, L. E., Phillips, P. E., Garris, P. A. and Wightman, R. M. (2007) Paradoxical modulation of short-term facilitation of dopamine release by dopamine autoreceptors. *J Neurochem*, **102**: 1115-1124.
83. Kitbunnadaj, R., Zuiderveld, O. P., de Esch, I. J., Vollinga, R. C., Bakker, R., Lutz, M., Spek, A. L., Cavoy, E., Deltent, M. F., Menge, W. M., Timmerman, H. and Leurs, R. (2003) Synthesis and structure-activity relationships of conformationally constrained histamine H(3) receptor agonists. *J Med Chem*, **46**: 5445-5457.
84. Koller EA, Cross JT, Doraiswamy PM, Malozowski SN (September 2003). "Pancreatitis associated with atypical antipsychotics: from the Food and Drug Administration's MedWatch surveillance system and published reports". *Pharmacotherapy* **23** (9): 1123–30.

85. Kroeze, W. K., Hufeisen, S. J., Popadak, B. A., Renock, S. M., Steinberg, S., Ernsberger, P., Jayathilake, K., Meltzer, H. Y. and Roth, B. L. (2003) H1-histamine receptor affinity predicts short-term weight gain for typical and atypical antipsychotic drugs. *Neuropsychopharmacology*, **28**: 519-526.
86. Kukreti, R., Tripathi, S., Bhatnagar, P., Gupta, S., Chauhan, C., Kubendran, S., Janardhan Reddy, Y. C., Jain, S. and Brahmachari, S. K. (2006) Association of DRD2 gene variant with schizophrenia. *Neurosci Lett*, **392**: 68-71.
87. Lesurtel M, Graf R, Aleil B, Walther DJ, Tian Y, Jochum W, Gachet C, Bader M, Clavien PA (2006). "Platelet-derived serotonin mediates liver regeneration". *Science* **312** (5770): 104–7.
88. Leweke, F.M.; Koethe, D.; Pahlisch, F.; Schreiber, D.; Gerth, C.W.; Nolden, B.M.; Klosterkötter, J.; Hellmich, M. et al. (2009). "S39-02 Antipsychotic effects of cannabidiol". *European Psychiatry* **24**: S207.
89. Lim, H. D., van Rijn, R. M., Ling, P., Bakker, R. A., Thurmond, R. L. and Leurs, R. (2005) Evaluation of histamine H1-, H2-, and H3-receptor ligands at the human histamine H4 receptor: identification of 4-methylhistamine as the first potent and selective H4 receptor agonist. *J Pharmacol Exp Ther*, **314**: 1310-1321.
90. Lindsley, Craig (17 March 2010). "GlyT1-Up from the Ashes. The Importance of Not Condemning a Mechanism Based on a Single Chemotype". *ACS Chemical Neuroscience* **1** (3): 165–166. Retrieved 6 October 2010
91. Liu, C., Ma, X., Jiang, X., Wilson, S. J., Hofstra, C. L., Blevitt, J., Pyati, J., Li, X., Chai, W., Carruthers, N. and Lovenberg, T. W. (2001) Cloning and pharmacological characterization of a fourth histamine receptor (H(4)) expressed in bone marrow. *Mol Pharmacol*, **59**: 420-426.
92. Liu, C., Wilson, S. J., Kuei, C. and Lovenberg, T. W. (2001) Comparison of human, mouse, rat, and guinea pig histamine H4 receptors reveals substantial pharmacological species variation. *J Pharmacol Exp Ther*, **299**: 121-130.
93. Maillet, M., Robert, S. J., Cacquevel, M., Gastineau, M., Vivien, D., Bertoglio, J., Zugaza, J. L., Fischmeister, R. and Lezoualc'h, F. (2003) Crosstalk between Rap1 and Rac regulates secretion of sAPPalpha. *Nat Cell Biol.*, **5**: 633-639.
94. Malmlöf, K., Zaragoza, F., Golozoubova, V., Refsgaard, H. H., Cremers, T., Raun, K., Wulff, B. S., Johansen, P. B., Westerink, B. and Rimvall, K. (2005) Influence of a selective histamine H3 receptor antagonist on

hypothalamic neural activity, food intake and body weight. Int J Obes (Lond), **29**: 1402-1412.

95. Manzanedo, C., Aguilar, M. A., Rodríguez-Arias, M. and Miñarro, J. (2005) Sensitization to the rewarding effects of morphine depends on dopamine. Neuroreport, **16**: 201-205.
96. Marieb, E. (2001). Human anatomy & physiology. San Francisco: Benjamin Cummings. pp. 414.
97. Maruko, T., Nakahara, T., Sakamoto, K., Saito, M., Sugimoto, N., Takuwa, Y. and Ishii, K. (2005) Involvement of the betagamma subunits of G proteins in the cAMP response induced by stimulation of the histamine H1 receptor. Naunyn Schmiedebergs Arch Pharmacol, **372**: 153-159.
98. Masaki, T., Chiba, S., Tatsukawa, H., Noguchi, H., Kakuma, T., Endo, M., Seike, M., Watanabe, T. and Yoshimatsu, H. (2005) The role of histamine H1 receptor and H2 receptor in LPS-induced liver injury. *FASEB J*, **19**: 1245-1252.
99. Matondo RB, Punt C, Homberg J, Toussaint MJ, Kisjes R, Korporaal SJ, Akkerman JW, Cuppen E, de Bruin A (2009). "Deletion of the serotonin transporter in rats disturbs serotonin homeostasis without impairing liver regeneration". *Am. J. Physiol. Gastrointest. Liver Physiol.* **296** (4): G963–8.
100. Matsubara, M., Ohmori, K. and Hasegawa, K. (2006) Histamine H1 receptor-stimulated interleukin 8 and granulocyte macrophage colony-stimulating factor production by bronchial epithelial cells requires extracellular signal-regulated kinase signaling via protein kinase C. Int Arch Allergy Immunol, **139**: 279-293.
101. Matsuda, N., Jesmin, S., Takahashi, Y., Hatta, E., Kobayashi, M., Matsuyama, K., Kawakami, N., Sakuma, I., Gando, S., Fukui, H., Hattori, Y. and Levi, R. (2004) Histamine H1 and H2 receptor gene and protein levels are differentially expressed in the hearts of rodents and humans. J Pharmacol Exp Ther, **309**: 786-795.
102. McKenna, F; McLaughlin, PJ; Lewis, BJ; Sibbring, GC; Cummerson, JA; Bowen-Jones, D; Moots, RJ. (2002). "Dopamine receptor expression on human T- and B-lymphocytes, monocytes, neutrophils, eosinophils and NK cells: a flow cytometric study". J Neuroimmunol **132** (1–2): 34–40.
103. Merims D, Giladi N (2008). "Dopamine dysregulation syndrome, addiction and behavioral changes in Parkinson's disease". Parkinsonism & Related Disorders **14** (4): 273–80.

104.Mignini, F; Streccioni, V; Amenta, F (2003). "Autonomic innervation of immune organs and neuroimmune modulation". Autonomic & autacoid pharmacology **23** (1): 1–25.

105.Millan, M. J., Gobert, A., Lejeune, F., Dekeyne, A., Newman-Tancredi, A., Pasteau, V., Rivet, J. M. and Cussac, D. (2003) The novel melatonin agonist agomelatine (S20098) is an antagonist at 5-hydroxytryptamine2C receptors, blockade of which enhances the activity of frontocortical dopaminergic and adrenergic pathways. J Pharmacol Exp Ther, **306**: 954-964.

106.Mödder UI, Achenbach SJ, Amin S, Riggs BL, Melton LJ 3rd, Khosla S (2010). "Relation of serum serotonin levels to bone density and structural parameters in women". *J Bone Miner Res.* **25** (2): 415–22.

107.Monroe EW, Daly AF, Shalhoub RF (February 1997). "Appraisal of the validity of histamine-induced wheal and flare to predict the clinical efficacy of antihistamines". *J. Allergy Clin. Immunol.* **99** (2): S798–806.

108.Mustard, J. A., Beggs, K. T. and Mercer, A. R. (2005) Molecular biology of the invertebrate dopamine receptors. *Arch Insect Biochem Physiol*, **59**: 103-117.

109.Narita, M., Mizuo, K., Mizoguchi, H., Sakata, M., Narita, M., Tseng, L. F. and Suzuki, T. (2003) Molecular evidence for the functional role of dopamine D3 receptor in the morphine-induced rewarding effect and hyperlocomotion. J Neurosci, **23**: 1006-1012.

110.Naunyn Schmiedebergs Arch. Pharmacol., **382** (4): 321-30.

111.Nelson DL (2004). *«*5-HT5 receptors*»*. Current drug targets. CNS and neurological disorders **3** (1): 53–8. Cinelli, A. R.; Efendiev, R.; Pedemonte, C. H. (2008). "Trafficking of Na-K-ATPase and dopamine receptor molecules induced by changes in intracellular sodium concentration of renal epithelial cells". *AJP:* Renal Physiology **295** (4): F1117–25.

112.Nelson, DL; Phebus, LA; Johnson, KW; Wainscott, DB; Cohen, ML; Calligaro, DO; Xu, YC. (2010) Preclinical pharmacological profile of the selective 5-HT1F receptor agonist lasmiditan. Cephalalgia, **30** (10): 1159-69.

113.Nelson, DL; Phebus, LA; Johnson, KW; Wainscott, DB; Cohen, ML; Calligaro, DO; Xu, YC. (2010) Preclinical pharmacological profile of the selective 5-HT1F receptor agonist lasmiditan. Cephalalgia, **30** (10): 1159-69.

114.Nemeroff CB, Lieberman JA, Weiden PJ, Harvey PD, Newcomer JW, Schatzberg AF, Kilts CD, Daniel DG. (November 2005). "From clinical

research to clinical practice: a 4-year review of ziprasidone". CNS Spectr **10** (11 Suppl 17): 1–20.

115.Olsen, DB; Eldrup, AB; Bartholomew, L; Bhat, B; Bosserman, MR; Ceccacci, A; Colwell, LF; Fay, JF et al. (2004). "A 7-Deaza-Adenosine Analog Is a Potent and Selective Inhibitor of Hepatitis C Virus Replication with Excellent Pharmacokinetic Properties". Antimicrobial agents and chemotherapy 48 (10): 3944–53.

116.Ouadid, H., Seguin, J., Dumuis, A., Bockaert, J. and Nargeot, J. (1992) Serotonin increases calcium current in human atrial myocytes via the newly described 5-hydroxytryptamine4 receptors. Mol Pharmacol., **41**: 346-351.

117.Ozono, R., O'Connell, D. P., Wang, Z. Q., Moore, A. F., Sanada, H., Felder, R. A. and Carey, R. M. (1997) Localization of the dopamine D1 receptor protein in the human heart and kidney. Hypertension, 30: 725-729.

118.Paterson DS, Trachtenberg FL, Thompson EG, Belliveau RA, Beggs AH, Darnall R, Chadwick AE, Krous HF, Kinney HC (2006). "Multiple serotonergic brainstem abnormalities in sudden infant death syndrome". JAMA **296** (17): 2124–32.

119.Patil ST, Zhang L, Martenyi F et al. (September 2007). "Activation of mGlu2/3 receptors as a new approach to treat schizophrenia: a randomized Phase 2 clinical trial". *Nature Medicine* **13** (9): 1102–7.

120.Paulmann N, Grohmann M, Voigt JP, Bert B, Vowinckel J, Bader M, Skelin M, Jevsek M, Fink H, Rupnik M, Walther DJ (2009). O'Rahilly, Steve. ed. "Intracellular serotonin modulates insulin secretion from pancreatic beta-cells by protein serotonylation". *PLoS Biol.* **7** (10): e1000229.

121.Ponimaskin, E. G., Profirovic, J., Vaiskunaite, R., Richter, D. W. and Voyno-Yasenetskaya, T. A. (2002) 5-Hydroxytryptamine 4(a) receptor is coupled to the Galpha subunit of heterotrimeric G13 protein. *J Biol Chem.*, **277**: 20812-20819.

122.Potrebic, S., Ahn, A. H., Skinner, K., Fields, H. L. and Basbaum, A. I. (2003) Peptidergic nociceptors of both trigeminal and dorsal root ganglia express serotonin 1D receptors: implications for the selective antimigraine action of triptans. *J Neurosci*, **23**: 10988-10997.

123.Ramage, AG; Villalón, CM. (2008) 5-hydroxytryptamine and cardiovascular regulation. *Trends Pharmacol. Sci.*, **29** (9): 472-81.

124.Richard A. Harvey, Pamela C. Champe. Pharmacology. 4th edition. Lippincott Williams & Wilkins. 2009. – 564p.

125.Sander, L. E., Lorentz, A., Sellge, G., Coëffier, M., Neipp, M., Veres, T., Frieling, T., Meier, P. N., Manns, M. P. and Bischoff, S. C. (2006) Selective expression of histamine receptors H1R, H2R, and H4R, but not H3R, in the human intestinal tract. *Gut*, **55**: 498-504.

126.Sarkar, C; Basu, B; Chakroborty, D; Dasgupta, PS; Basu, S (2010). "The immunoregulatory role of dopamine: an update". *Brain, behavior, and immunity* **24** (4): 525–8.

127.Schaerlinger, B., Hickel, P., Etienne, N., Guesnier, L. and Maroteaux, L. (2003) Agonist actions of dihydroergotamine at 5-HT2B and 5-HT2C receptors and their possible relevance to antimigraine efficacy. *Br J Pharmacol*, **140**: 277-284.

128.Schetz, J.A. and Sibley, D.R. (2007) Dopaminergic Neurotransmission. *in* Handbook of Contemporary Neuropharmacology *Edited by* David Sibley, Isreal Hanin, Michael Kuhar, Phil Skolnick John Wiley & Sons, Inc.. 221-256

129.Schnurr, M., Toy, T., Shin, A., Hartmann, G., Rothenfusser, S., Soellner, J., Davis, I. D., Cebon, J. and Maraskovsky, E. (2004) Role of adenosine receptors in regulating chemotaxis and cytokine production of plasmacytoid dendritic cells. *Blood*, **103**: 1391-1397.

130.Schweda, F., Segerer, F., Castrop, H., Schnermann, J. and Kurtz, A. (2005) Blood pressure-dependent inhibition of Renin secretion requires A1 adenosine receptors. *Hypertension*, **46**: 780-786.

131.Sidorenko B.A., D.V. Preobrazhensky. α-Adrenoceptor blockers as antihypertensives /Русский медицинский журнал. №8. 2012.

132.Soyka, M., Preuss, U. W., Koller, G., Zill, P. and Bondy, B. (2004) Association of 5-HT1B receptor gene and antisocial behavior in alcoholism. *J Neural Transm*, **111**: 101-109.

133.Stein C, Schäfer M, Machelska H (2003) Attacking pain at its source: new perspectives on opioids. Nature Med;9(8):1003-1008.

134.Stephen J. Hill, Paul Chazot, Hiroyuki Fukui, C. Robin Ganellin, Helmut L. Haas, Rebecca Hills, Roberto Levi, Walter Schunack, Jean-Charles Schwartz, Nigel P. Shankley, Henk Timmerman, J. Michael Young. Histamine receptors, introductory chapter. Accessed on 27/06/2012. IUPHAR database (IUPHAR-DB), http://www.iuphar-db.org/DATABASE/FamilyIntroductionForward?familyId=33.

135.Sugimoto, H., Shichijo, M., Iino, T., Manabe, Y., Watanabe, A., Shimazaki, M., Gantner, F. and Bacon, K. B. (2003) An orally bioavailable small molecule antagonist of CRTH2, ramatroban (BAY u3405), inhibits

prostaglandin D2-induced eosinophil migration in vitro. *J Pharmacol Exp* Ther, 305: 347-352.

136.Sun, W. C., Jin, L., Cao, Y., Wang, L. Z., Meng, F. and Zhu, X. Z. (2005) Cloning, expression, and functional analysis of human dopamine D1 receptors. *Acta Pharmacol Sin*, **26**: 27-32.

137.Swainston Harrison T, Perry CM (2004). "Aripiprazole: a review of its use in schizophrenia and schizoaffective disorder". *Drugs* **64** (15): 1715–36.

138.Terzioglu, N., van Rijn, R. M., Bakker, R. A., de Esch, I. J. and Leurs, R. (2004) Synthesis and structure-activity relationships of indole and benzimidazole piperazines as histamine H(4) receptor antagonists. *Bioorg Med Chem Lett*, **14**: 5251-5256.

139.The Eicosanoids. Peter Curtis-Prior (Editor). Hardcover. 654 p., 2004.

140.Tokita, S., Takahashi, K. and Kotani, H. (2006) Recent advances in molecular pharmacology of the histamine systems: physiology and pharmacology of histamine H3 receptor: roles in feeding regulation and therapeutic potential for metabolic disorders. *J Pharmacol Sci*, **101**: 12-18.

141.Torres, G. E., Holt, I. L. and Andrade, R. (1994) Antagonists of 5-HT4 receptor-mediated responses in adult hippocampal neurons. *J Pharmacol Exp Ther.*, **271**: 255-261.

142.Torrey EF, Swalwell CI (December 2003). "Fatal olanzapine-induced ketoacidosis". *The American Journal of Psychiatry* **160** (12): 2241.

143.Trist, D. G., Collins, B. A., Wood, J., Kelly, M. G. and Robertson, A. D. (1989) The antagonism by BW A868C of PGD_2 and BW245C activation of human platelet adenylate cyclase. *Br. J. Pharmacol.*, **96**: 301-306.

144.Valent P, Horny HP, Escribano L, *et al.* (July 2001). "Diagnostic criteria and classification of mastocytosis: a consensus proposal". *Leuk. Res.* **25** (7): 603–25.

145.Varnas, K., Hurd, Y. L. and Hall, H. (2005) Regional expression of 5-HT1B receptor mRNA in the human brain. *Synapse*, **56**: 21-28.

146.Varty, L. M., Gustafson, E., Laverty, M. and Hey, J. A. (2004) Activation of histamine H3 receptors in human nasal mucosa inhibits sympathetic vasoconstriction. *Eur J Pharmacol*, **484**: 83-89.

147.Villalón, CM; Centurión, D. (2007) Cardiovascular responses produced by 5-hydroxytriptamine:a pharmacological update on the receptors/mechanisms involved and therapeutic implications. *Naunyn Schmiedebergs Arch. Pharmacol.*, **376** (1-2): 45-63.

148.White, JM; Rumbold, GR (1988). "Behavioural effects of histamine and its antagonists: a review.". *Psychopharmacology* **95** (1): 1–14.

149.Wieland, K., Bongers, G., Yamamoto, Y., Hashimoto, T., Yamatodani, A., Menge, W. M., Timmerman, H., Lovenberg, T. W. and Leurs, R. (2001) Constitutive activity of histamine h(3) receptors stably expressed in SK-N-MC cells: display of agonism and inverse agonism by H(3) antagonists. *J Pharmacol Exp Ther*, **299**: 908-914.

150.Wood, PB. (2008). "Role of central dopamine in pain and analgesia". *Expert Rev Neurother* **8** (5): 781–97.

151.Wood, PB; Schweinhardt, P; Jaeger, E; Dagher, A; Hakyemez, H; Rabiner, EA; Bushnell, MC; Chizh, BA. (2007). "Fibromyalgia patients show an abnormal dopamine response to pain". *Eur J Neurosci* **25** (12): 3576–82.

152.Woodward, D. F., Nieves, A. L. and Friedlaender, M. H. (1996) Characterization of receptor subtypes involved in prostanoid-induced conjunctival pruritus and their role in mediating allergic conjunctival itching. *J Pharmacol Exp Ther*, **279**: 137-142.

153.Wulff, B. S., Hastrup, S. and Rimvall, K. (2002) Characteristics of recombinantly expressed rat and human histamine H3 receptors. *Eur J Pharmacol*, **453**: 33-41.

154.Xu, F; Wu, H; Katritch, V; Han, GW; Jacobson, KA; Gao, ZG; Cherezov, V; Stevens, RC. (2011) Structure of an agonist-bound human A2A adenosine receptor. *Science*, **332** (6027): 322-7.

155.Yadav VK, Balaji S, Suresh PS, Liu XS, Lu X, Li Z, Guo XE, Mann JJ, Balapure AK, Gershon MD, Medhamurthy R, Vidal M, Karsenty G, Ducy P. (2010). "Pharmacological inhibition of gut-derived serotonin synthesis is a potential bone anabolic treatment for osteoporosis". *Nat Med.* **16** (3): 308–12.

156.Yadav VK, Ryu JH, Suda N, Tanaka KF, Gingrich JA, Schütz G, Glorieux FH, Chiang CY, Zajac JD, Insogna KL, Mann JJ, Hen R, Ducy P, Karsenty G (2008). "Lrp5 controls bone formation by inhibiting serotonin synthesis in the duodenum". *Cell* **135** (5): 825–37.

157.Yanai, K; Tashiro, M (2007). "The physiological and pathophysiological roles of neuronal histamine: an insight from human positron emission tomography studies.". *Pharmacology & therapeutics* **113** (1): 1–15.

158.Yoshimura-Uchiyama, C., Iikura, M., Yamaguchi, M., Nagase, H., Ishii, A., Matsushima, K., Yamamoto, K., Shichijo, M., Bacon, K. B. and Hirai, K. (2004) Differential modulation of human basophil functions through prostaglandin D2 receptors DP and chemoattractant receptor-homologous molecule expressed on Th2 cells/DP2. *Clin Exp Allergy*, **34**: 1283-1290.

159.Young SN (2007). "How to increase serotonin in the human brain without drugs". *Rev. Psychiatr. Neurosci.* **32** (6): 394–99.

160.Zeng, C., Zhang, M., Asico, L. D., Eisner, G. M. and Jose, P. A. (2007) The dopaminergic system in hypertension. *Clin Sci (Lond)*, **112**: 583-597.

161.Zhu, Y., Michalovich, D., Wu, H., Tan, K. B., Dytko, G. M., Mannan, I. J., Boyce, R., Alston, J., Tierney, L. A., Li, X., Herrity, N. C., Vawter, L., Sarau, H. M., Ames, R. S., Davenport, C. M., Hieble, J. P., Wilson, S., Bergsma, D. J. and Fitzgerald, L. R. (2001) Cloning, expression, and pharmacological characterization of a novel human histamine receptor. *Mol Pharmacol*, **59**: 434-441.

162.Zuardi AW, Crippa JA, Hallak JE, Moreira FA, Guimarães FS (April 2006). "Cannabidiol, a Cannabis sativa constituent, as an antipsychotic drug". *Brazilian Journal of Medical and Biological Research* **39** (4): 421–9.

Германюк Т.А., Бобрук В.П., Лисогора В.В.

ФАРМАКОЛОГІЯ лікарських засобів, які впливають на медіаторні процеси, вегетативну та центральну нервову систему

НАВЧАЛЬНИЙ ПОСІБНИК

на англійській мові

Підписано до друку 10.09.15.
Формат 84х60/16. Папір офсетний.
Друк офсетний. Гарнітура Times New Roman.
Умов. друк. арк. 20,87. Обл.-вид. арк. 19,41.
Наклад 100 прим. Зам. № 9790.

Віддруковано з оригіналів замовника.
ФОП Корзун Д.Ю.

Видавець та виготовлювач ТОВ «Нілан-ЛТД»
Свідоцтво про внесення суб'єкта видавничої справи до
Державного реєстру видавців, виготовлювачів і розповсюджувачів
видавничої продукції серія DK № 4299 від 11.04.2012 р.
21027, а/я 8825, м. Вінниця, вул. 600-річчя, 21.
Тел.: (0432) 69-67-69, 603-000.