

REFERENCES:

- Abou-Khalil B., "Levetiracetam in the Treatment of Epilepsy," *Neuropsychiatric Disease and Treatment*, (3),**4**(2008)507.
- Acharya C., Coop A., Polli J.E., and MacKerell AD Jr., "Recent Advances in Ligand-Based Drug Design: Relevance and Utility of the Conformationally Sampled Pharmacophore Approach," *Current Computer-Aided Drug Design*, (1),**7**(2011)10-22.
- Althaus J.S. and Martin D.L., "Entropy as a Factor in the Binding of γ -aminobutyric acid and Nipecotic Acid to the γ -aminobutyric Acid Transport System," *Neurochemical Research*, (4),**14**(1989)311-316.
- Ambrósio A.F., Silva A.P., Araújo I., Malva J.O., Soares-da-Silva P.C., Carvalho A.P. and Carvalho C.M., "Neurotoxic/neuroprotective Profile of Carbamazepine, Oxcarbazepine and Two New Putative Antiepileptic Drugs, BIA 2-093 and BIA 2-024," *European Journal of Pharmacology*, (2),**406**(2000)191-201.
- Ambrósio A.F., Soares-da-Silva P., Carvalho C.M. and Carvalho A.P., "Mechanisms of Action of Carbamazepine and its Derivatives, Oxcarbazepine, BIA 2-093, and BIA 2-024," *Neurochemical Research*, (1-2),**27**(2002)121-130.
- Andersen K.E., Lau J., Lundt B.F., Petersen H., Huusfeldt P.O., Suzdak P.D. and Swedberg M.D., "Synthesis of novel GABA uptake inhibitors. part 6†: Preparation and Evaluation of N- Ω asymmetrically Substituted Nipecotic Acid Derivatives," *Bioorganic & Medicinal Chemistry*, (11),**9**(2001)2773-2785.
- Andersen K.E., Sørensen J.L., Lau J., Lundt B.F., Petersen H., Huusfeldt P.O., Suzdak P.D. and Swedberg M.D., "Synthesis of Novel γ -Aminobutyric Acid (GABA) Uptake Inhibitors. 5. Preparation and Structure– Activity Studies of Tricyclic Analogues of Known GABA Uptake Inhibitors," *Journal of Medicinal Chemistry*, (13),**44**(2001a)2152-2163.
- Ängehagen M., Ben-Menachem E., Rönnbäck L. and Hansson E., "Novel Mechanisms of Action of Three Antiepileptic Drugs, Vigabatrin, Tiagabine, and Topiramate," *Neurochemical Research*, (2),**28**(2003)333-340.
-

- Araújo I.M., Ambrósio A.F., Leal E.C., Verdasca M.J., Malva J.O., Soares-da-Silva P., Carvalho A.P. and Carvalho C.M., "Neurotoxicity Induced by Antiepileptic Drugs in Cultured Hippocampal Neurons: A Comparative Study between Carbamazepine, Oxcarbazepine, and Two New Putative Antiepileptic Drugs, BIA 2-024 and BIA 2-093," *Epilepsia*, (12),**45**(2004)1498-1505.
- Ashton H., "Adverse Effects of Prolonged Benzodiazepine Use," *Adverse Drug Reaction Bulletin*, (1),**118**(1986)440-443.
- Aydemir N., Kaya B., Yıldız G., Öztura İ. and Baklan B., "Determinants of Felt Stigma in Epilepsy," *Epilepsy & Behavior*, **58**(2016)76-80.
- Bachmann, T., Bertheussen, K., Svalheim, S., Rauchenzauner, M., Luef, G., Gjerstad, L. and Taubøll, E., "Haematological Side Effects of Antiepileptic Drug Treatment in Patients With Epilepsy", *Acta Neurologica Scandinavica*, **124**(2011), 23-27.
- Banerjee A.G., Das N., Shengule S.A., Sharma P.A., Srivastava R.S. and Shrivastava S.K., "Design, Synthesis, Evaluation and Molecular Modelling Studies of Some Novel 5, 6-diphenyl-1, 2, 4-triazin-3 (2H)-ones Bearing Five-Member Heterocyclic Moieties as Potential COX-2 Inhibitors: A hybrid Pharmacophore Approach," *Bioorganic Chemistry*, **69**(2016)102-120.
- Barrett-Jolley R., "Nipecotic Acid Directly Activates GABAA-Like Ion Channels," *British Journal of Pharmacology*, (5),**133**(2001)673-678.
- Bauer J. and Cooper-Mahkorn D., "Tiagabine: Efficacy and Safety in Partial Seizures—Current Status," *Neuropsychiatric Disease and Treatment*, (4),**4**(2008)731.
- Baybaş S., Yıldırım Z., Ertem D.H., Dirican A. and Dirican A., "Development and Validation of The Stigma Scale for Epilepsy in Turkey," *Epilepsy & Behavior*, **67**(2017)84-90.
- Benke D., Zemoura K. and Maier P.J., "Modulation of Cell Surface GABAB Receptors by Desensitization, Trafficking and Regulated Degradation," *World Journal of Biological Chemistry*, (4),**3**(2012)61.

- Ben-Menachem E., "Mechanism of Action of Vigabatrin: Correcting Misperceptions," *Acta Neurologica Scandinavica*, (s192),**124**(2011)5-15.
- Bettler B., Kaupmann K., Mosbacher J. and Gassmann M., "Molecular Structure and Physiological Functions of GABAB Receptors," *Physiological Reviews*, (3),**84**(2004)835-867.
- Bialer M. and Yagen B., "Valproic acid: Second Generation," *Neurotherapeutics*, (1),**4**(2007)130-137.
- Bjorge S., Black A., Bockbrader H., Chang T., Gregor V.E., Lobbstaal S.J., Nugiel D., Pavia M.R., Radulovic L. and Woolf T., "Synthesis and Metabolic Profile of CI-966: A Potent, Orally-Active Inhibitor of GABA Uptake," *Drug Development Research*, (3),**21**(1990)189-193.
- Bonansco C. and Fuenzalida M., "Plasticity of Hippocampal Excitatory-Inhibitory Balance: Missing the Synaptic Control in The Epileptic Brain," *Neural Plasticity*, **2016**(2016)1-16.
- Bonina F.P., Arenare L., Palagiano F., Saija A., Nava F., Trombetta D. and Caprariis P.D., "Synthesis, Stability, and Pharmacological Evaluation of Nipecotic Acid Prodrugs," *Journal of Pharmaceutical Sciences*, (5),**88**(1999)561-567.
- Bourin M. and Briley M., "Sedation, an Unpleasant, Undesirable and Potentially Dangerous Side-Effect of Many Psychotropic Drugs," *Human Psychopharmacology: Clinical and Experimental*, (2),**19**(2004)135-139.
- Braestrup C., "Modulation of GABA Receptor Interaction With GABA Uptake Inhibitors," *Pharmacology*, (1987)125-128.
- Braestrup C., Nielsen E.B., Sonnewald U., Knutsen L.J., Andersen K.E., Jansen J.A., Frederiksen K., Andersen P.H., Mortensen A. and Suzdak P.D., "(R)-N-[4, 4-Bis (3-Methyl-2-Thienyl) but-3-en-1-yl] Nipecotic Acid Binds with High Affinity to the Brain γ -Aminobutyric Acid Uptake Carrier," *Journal of Neurochemistry*, (2),**54**(1990)639-647.

- Bromfield E.B., Cavazos J.E. and Sirven J.I., Basic Mechanisms Underlying Seizures and Epilepsy, American Epilepsy Society, West Hartford (CT), 2006.
- Çalış Ü., Dalkara S., Ertan M. and Sunal R., "The Significance of The Imidazole Ring in Anticonvulsant Activity of (Arylalkyl) Imidazoles," *Archiv der Pharmazie*, (12),**321**(1988)841-846.
- Chebib M. and Johnston G.A., "Stimulation of [3H] GABA and β -[3H] Alanine Release from Rat Brain Slices by cis-4-Aminocrotonic Acid," *Journal of Neurochemistry*, (2),**68**(1997)786-794.
- Chen N.-H., Reith M.E. and Quick M.W., "Synaptic Uptake and Beyond: The Sodium-and Chloride-Dependent Neurotransmitter Transporter Family SLC6," *Pflügers Archiv*, (5),**447**(2004)519-531.
- Corey J.L., Guastella J., Davidson N. and Lester H.A., "GABA Uptake and Release by a Mammalian Cell Line Stably Expressing a Cloned Rat Brain GABA Transporter," *Molecular Membrane Biology*, (1),**11**(1994)23-30.
- Coulter D.A., "Antiepileptic Drug Cellular Mechanisms of Action: Where Does Lamotrigine Fit in?," *Journal of Child Neurology*, (1_suppl),**12**(1997)S2-S9.
- Curia G., Longo D., Biagini G., Jones R.S. and Avoli M., "The Pilocarpine Model of Temporal Lobe Epilepsy," *Journal of Neuroscience Methods*, (2),**172**(2008)143-157.
- Czapinski P., Blaszczyk B. and Czuczwar S. J., "Mechanisms of Action of Antiepileptic Drugs", *Current Topics in Medicinal Chemistry*, (1),**5**(2005)3-14.
- Das N., Dhanawat M. and Shrivastava S.K., "An Overview on Antiepileptic Drugs," *Drug Discoveries & Therapeutics*, (4),**6**(2012)178-193.
- Das N., Garabadu D., Banerjee A.G., Krishnamurthy S. and Shrivastava S.K., "Synthesis and Pharmacological Evaluation of Some N3-aryl/heteroaryl-substituted 2-(2-chlorostyryl)-6, 7-Dimethoxy-Quinazolin-4 (3H)-ones as Potential Anticonvulsant agents," *Medicinal Chemistry Research*, (9),**23**(2014)4167-4176.

- De Deyn P.P., D'Hooge R., Marescau B. and Pei Y.-Q., "Chemical Models of Epilepsy With Some Reference to Their Applicability in the Development of Anticonvulsants," *Epilepsy Research*, (2),**12**(1992)87-110.
- Del Arco A., Castaneda T.R. and Mora F., "Amphetamine Releases GABA in Striatum of the Freely Moving Rat: Involvement of Calcium and High Affinity Transporter Mechanisms," *Neuropharmacology*, (2),**37**(1998)199-205.
- Di L., Kerns E.H., Fan K., McConnell O.J. and Carter G.T., "High Throughput Artificial Membrane Permeability Assay for Blood–Brain Barrier," *European Journal of Medicinal Chemistry*, (3),**38**(2003)223-232.
- Enz R., "GABAC Receptors: a Molecular View," *Biological Chemistry*, (8),**382**(2001)1111-1122.
- Falch E. and Krogsgaard-Larsen P., "GABA Uptake Inhibitors Containing Mono-and Diarylmethoxyalkyl N-Substituents," *Drug Design and Delivery*, (3),**4**(1989)205-215.
- Farrant M. and Nusser Z., "Variations on an Inhibitory Theme: Phasic and Tonic Activation of GABA A Receptors," *Nature Reviews Neuroscience*, (3),**6**(2005)215.
- Fraga C.A.M., "Drug Hybridization Strategies: Before or after Lead Identification?," *Expert Opinion on Drug Discovery*, (6),**4**(2009)605-609.
- Freifelder M. and Stone G.R., "Reductions with Ruthenium. II. Its Use in the Hydrogenation of Pyridines1," *The Journal of Organic Chemistry*, (10),**26**(1961)3805-3808.
- Freifelder M., "A Simple Preparation of Nipecotic Acid," *The Journal of Organic Chemistry*, (4),**28**(1963)1135-1135.
- Freifelder M., "Hydrogenation of Pyridinecarboxylic Acids with Platinum Catalyst," *The Journal of Organic Chemistry*, (11),**27**(1962)4046-4046.

- Freifelder M., Robinson R.M. and Stone G.R., "Hydrogenation of Substituted Pyridines with Rhodium on Carbon Catalyst1," *The Journal of Organic Chemistry*, (1),**27**(1962)284-286.
- Friedman H.L., "Influence of Isosteric Replacements upon Biological Activity," *National Academy of Science-National Research Council Publication*, **206**(1951)295-358.
- Gao X.M. and Chuang D.M., "Carbamazepine-Induced Neurotoxicity and its Prevention by NMDA in Cultured Cerebellar Granule Cells," *Neuroscience Letters*, (2),**135**(1992)159-162.
- Gao X.M., Margolis R.L., Leeds P., Hough C., Post R.M. and Chuang D.M., "Carbamazepine Induction of Apoptosis in Cultured Cerebellar Neurons: Effects of n-Methyl-D-Aspartate, Aurintricarboxylic Acid and Cycloheximide," *Brain Research*, (1-2),**703**(1995)63-71.
- Ghadimi S., Latif Mousavi S. and Javani Z., "Synthesis, Lipophilicity Study and *in vitro* Evaluation of Some Rodenticides as Acetylcholinesterase Reversible Inhibitors," *Journal of Enzyme Inhibition and Medicinal Chemistry*, (2),**23**(2008)213-217.
- Ghareb N., Daim M.M.A., El-Sayed N.M. and Elgawish M.S., "Synthesis, Molecular Modelling, and Preliminary Anticonvulsant Activity Evaluation of Novel Naphthalen-2-yl Acetate and 1, 6-Dithia-4, 9-Diazaspiro [4.4] Nonane-3, 8-Dione Derivatives," *Bioorganic Chemistry*, **71**(2017)110-119.
- Goldenberg M.M., "Overview of Drugs Used For Epilepsy and Seizures: Etiology, Diagnosis, and Treatment," *Pharmacy and Therapeutics*, (7),**35**(2010)392.
- Gören M.Z. and Onat F., "Ethosuximide: From Bench to Bedside," *CNS Drug Reviews*, (2),**13**(2007)224-239.
- Gram, L. and Bentsen, K. D., "Hepatic Toxicity of Antiepileptic Drugs: A Review", *Acta Neurologica Scandinavica*, **68** (1983), 81-90.

- Gunthorpe M.J., Large C.H. and Sankar R., "The Mechanism of Action of Retigabine (Ezogabine), A First-in-class K⁺ Channel Opener for the Treatment of Epilepsy," *Epilepsia*, (3),**53**(2012)412-424.
- Gustavson L.E. and Mengel H.B., "Pharmacokinetics of Tiagabine, a γ -Aminobutyric Acid-Uptake Inhibitor, in Healthy Subjects After Single and Multiple Doses," *Epilepsia*, (6),**36**(1995)605-611.
- Hamed, S. A., "The Effect of Antiepileptic Drugs on the Kidney Function and Structure," *Expert Review of Clinical Pharmacology*, (9)**10** (2017), 993-1006.
- Hellenbrand T., Höfner G., Wein T. and Wanner K.T., "Synthesis of 4-Substituted Nipecotnic Acid Derivatives and Their Evaluation as Potential GABA Uptake Inhibitors," *Bioorganic & Medicinal Chemistry*, (9),**24**(2016)2072-2096.
- Hinko C., Crider A., Kliem M., Steinmiller C., Seo T., Ho B., Venkatarangan P., El-Assadi A., Chang H. and Burns C., "Anticonvulsant Activity of Novel Derivatives of 2-and 3-Piperidinecarboxylic Acid in Mice and Rats," *Neuropharmacology*, (12),**35**(1996)1721-1735.
- Hoesl C.E., Höfner G. and Wanner K.T., "First Asymmetric Syntheses of 6-Substituted Nipecotnic Acid Derivatives," *Tetrahedron*, (2),**60**(2004)307-318.
- Huang H.J., Lee K.J., Yu H.W., Chen C.Y., Hsu C.H., Chen H.Y., Tsai F.J. and Chen C.Y.C., "Structure-Based and Ligand-Based Drug Design for HER 2 Receptor," *Journal of Biomolecular Structure and Dynamics*, (1),**28**(2010)23-37.
- Hunter W., Quinton R., Sherman P., Worthing C. and Boscott R., "The Anticonvulsant Activities of Some Substituted Acetonaphthones," *Journal of Medicinal Chemistry*, (2),**7**(1964)167-174.
- Jacoby A., Snape D. and Baker G.A., "Epilepsy and Social Identity: The Stigma of a Chronic Neurological Disorder," *The Lancet Neurology*, **4**(2005)171-178.

- Jiang G., Zhuang L., Miyauchi S., Miyake K., Fei Y.J. and Ganapathy V., "A Na⁺/Cl⁻-Coupled GABA Transporter, GAT-1, from *Caenorhabditis Elegans* Structural and Functional Features, Specific Expression in Gaba-Ergic Neurons, and Involvement in Muscle Function," *Journal of Biological Chemistry*, (3),**280**(2005)2065-2077.
- Johnston G., Krogsgaard-Larsen P., Stephanwn A. and Twitchin B., "Inhibition of the Uptake of GABA and Related Amino Acids in Rat Brain Slices by the Optical Isomers of Nipecotnic Acid," *Journal of Neurochemistry*, (5),**26**(1976)1029-1032.
- Jurik A., Reicherstorfer R., Zdrzil B. and Ecker G.F., "Classification of High-Activity Tiagabine Analogs by Binary QSAR Modeling," *Molecular Informatics*, (5-6),**32**(2013)415-419.
- Jurik A., Zdrzil B., Holy M., Stockner T., Sitte H.H. and Ecker G.F., "A Binding Mode Hypothesis of Tiagabine Confirms Liothyronine Effect on γ -aminobutyric acid Transporter 1 (GAT1)," *Journal of Medicinal Chemistry*, (5),**58**(2015)2149-2158.
- Karakurt A., Aytemir M.D., Stables J.P., Özalp M., Betül Kaynak F., Özbey S. and Dalkara S., "Synthesis of Some Oxime Ether Derivatives of 1-(2-Naphthyl)-2-(1, 2, 4-triazol-1-yl) Ethanone and Their Anticonvulsant and Antimicrobial Activities," *Archiv der Pharmazie*, (9),**339**(2006)513-520.
- Karakurt A., Özalp M., Işık Ş., Stables J.P. and Dalkara S., "Synthesis, Anticonvulsant and Antimicrobial Activities of Some New 2-Acetylnaphthalene Derivatives," *Bioorganic & Medicinal Chemistry*, (8),**18**(2010)2902-2911.
- Kellinghaus C., "Lacosamide as Treatment for Partial Epilepsy: Mechanisms of Action, Pharmacology, Effects, and Safety," *Therapeutics and Clinical Risk Management*, **5**(2009)757.
- Kerwin R. and Taberner P., "The Mechanism of Action of Sodium Valproate," *General Pharmacology: The Vascular System*, (2),**12**(1981)71-75.

- Kim M. and Cho A.E., "Incorporating QM and Solvation into Docking for Applications to GPCR Targets," *Physical Chemistry Chemical Physics*, (40),**18**(2016)28281-28289.
- King L.C. and Ostrum G.K., "Selective Bromination with Copper (II) Bromide," *The Journal of Organic Chemistry*, (12),**29**(1964)3459-3461.
- Knutsen L.J., Andersen K.E., Lau J., Lundt B.F., Henry R.F., Morton H.E., Nærum L., Petersen H., Stephensen H. and Suzdak P.D., "Synthesis of Novel GABA Uptake inhibitors. 3. Diaryloxime and Diarylvinyl Ether Derivatives of Nipectic Acid and Guvacine as Anticonvulsant Agents," *Journal of Medicinal Chemistry*, (18),**42**(1999)3447-3462.
- Kowalczyk P., Sałat K., Höfner G.C., Mucha M., Rapacz A., Podkowa A., Filipek B., Wanner K.T. and Kulig K., "Synthesis, Biological Evaluation and Structure–Activity Relationship of New GABA Uptake Inhibitors, Derivatives of 4-Aminobutanamides," *European Journal of Medicinal Chemistry*, **83**(2014)256-273.
- Krogsgaard-Larsen P. and Johnston G., "Inhibition of GABA Uptake in Rat Brain Slices by Nipectic Acid, Various Isoxazoles and Related Compounds," *Journal of Neurochemistry*, (6),**25**(1975)797-802.
- Krogsgaard-Larsen P., "Inhibitors of the GABA Uptake Systems," *Molecular and Cellular Biochemistry*, (2),**31**(1980)105-121.
- Kubova H. *Antiepileptic Drug Discovery*, pp. 329-350, Springer, 2016.
- Kulick C.V., Gutherz S.B., Beck V.C., Medvedeva N., Soper C. and Forcelli P.A., "Profile of Anticonvulsant Action of Levetiracetam, Tiagabine and Phenobarbital Against Seizures Evoked by DMCM (methyl-6, 7-dimethoxy-4-ethyl- β -carboline-3-carboxylate) in Neonatal Rats," *European Journal of Pharmacology*, **743**(2014)63-68.
- Kulkarni S. and Joseph P., "Psychopharmacological Profile of Siotone Granules, a Herbal Preparation," *Indian Drugs*, (9),**35**(1998)536-544.

- Kumar S. and Pathak D.P., "Synthesis, Characterization and Evaluation for Anticonvulsant Activity of Acetylnaphthalene and Substituted Acetylenaphthalene Derivative Of Heterocyclic Compounds," *The Pharma Innovation*, (11),**1**(2013)90-101.
- Larsson O.M. and Schousboe A., "Comparison Between (RS)-Nipecotic Acid and GABA Transport In Cultured Astrocytes: Coupling with Two Sodium Ions," *Neurochemical Research*, (3),**6**(1981)257-266.
- Lee D., Steingard R., Cesena M., Helmers S., Riviello J. and Mikati M., "Behavioral Side Effects of Gabapentin in Children," *Epilepsia*, (1),**37**(1996)87-90.
- Leppik I.E., "Zonisamide: Chemistry, Mechanism of Action, And Pharmacokinetics," *Seizure-European Journal of Epilepsy*, **13**(2004)S5-S9.
- Levinson D.F. and Devinsky O., "Psychiatric Adverse Events During Vigabatrin Therapy," *Neurology*, (7),**53**(1999)1503-1503.
- Lim S.W., Loh H.S., Ting K.N., Bradshaw T.D. and Allaudin Z.N., "Reduction of MTT to Purple Formazan by Vitamin E Isomers in The Absence of Cells," *Tropical Life Sciences Research*, (1),**26**(2015)111.
- Lima L.M. and Barreiro E.J., "Bioisosterism: a Useful Strategy for Molecular Modification and Drug Design," *Current Medicinal Chemistry*, (1),**12**(2005)23-49.
- Lipinski C.A., Lombardo F., Dominy B.W. and Feeney P.J., "Experimental and Computational Approaches to Estimate Solubility and Permeability in Drug Discovery and Development Settings," *Advanced Drug Delivery Reviews*, **64**(2012)4-17.
- Liu Q.R., Lopez-Corcuera B., Mandiyan S., Nelson H. and Nelson N., "Molecular Characterization of Four Pharmacologically Distinct Gamma-Aminobutyric Acid Transporters in Mouse Brain," *Journal of Biological Chemistry*, (3),**268**(1993)2106-2112.

- Liu Y., Wang X.Y., Li D., Yang L. and Huang S.P., "Short-Term Use of Antiepileptic Drugs is Neurotoxic to the Immature Brain," *Neural Regeneration Research*, (4),**10**(2015)599-604.
- Löscher W., "Critical Review of Current Animal Models of Seizures and Epilepsy Used in the Discovery and Development of New Antiepileptic Drugs," *Seizure-European Journal of Epilepsy*, (5),**20**(2011)359-368.
- Löscher W. and Schmidt, D., "Modern Antiepileptic Drug Development Has Failed to Deliver: Ways Out of the Current Dilemma". *Epilepsia*, **52**(2011)657-678.
- Lutz, T., Wein, T., Höfner, G. and Wanner, K.T., "Development of Highly Potent GAT1 Inhibitors: Synthesis of Nipecotic Acid Derivatives with N-Arylalkynyl Substituents," *ChemMedChem*, (5),**12**(2017)362-371.
- Macalino S.J.Y., Gosu V., Hong S. and Choi S., "Role of Computer-Aided Drug Design in Modern Drug Discovery," *Archives of Pharmacal Research*, (9),**38**(2015)1686-1701.
- Macdonald R. L. & Kelly K. M., "Antiepileptic Drug Mechanisms of Action". *Epilepsia*, (Suppl.2),**36**(1995)S2-S12.
- Madtes P. and Redburn D.A., "Intraocular Injections of Nipecotic Acid Produce A Preferential Block of Neuronal 3H-GABA Accumulation in Adult Rabbit Retina," *Investigative Ophthalmology & Visual Science*, (7),**24**(1983)886-892.
- Malchow R.P. and Ripps H., "Effects of Gamma-Aminobutyric Acid on Skate Retinal Horizontal Cells: Evidence for an Electrogenic Uptake Mechanism," *Proceedings of the National Academy of Sciences*, (22),**87**(1990)8945-8949.
- Martis E.A. and Somani R.R., "Drug Designing, Discovery and Development Techniques" Promising Pharmaceuticals, InTech, Rijeka, 2012.
- Meena P., Nemaysh V., Khatri M., Manral A., Luthra P.M. and Tiwari M., "Synthesis, Biological Evaluation and Molecular Docking Study of Novel Piperidine and Piperazine

- Derivatives as Multi-Targeted Agents to Treat Alzheimer's Disease," *Bioorganic and Medicinal Chemistry*, (5),**23**(2015)1135-1148.
- Megiddo I., Colson A., Chisholm D., Dua T., Nandi A. and Laxminarayan R., "Health and Economic Benefits of Public Financing of Epilepsy Treatment in India: An Agent-Based Simulation Model," *Epilepsia*, (3),**57**(2016)464-474.
- Meldrum B.S. and Chapman A.G., "Basic Mechanisms of Gabitril (Tiagabine) and Future Potential Developments," *Epilepsia*, (s9),**40**(1999)S2-6.
- Michelini S., Cassano G., Frare F. and Perugi G., "Long-Term Use of Benzodiazepines: Tolerance, Dependence and Clinical Problems in Anxiety and Mood Disorders," *Pharmacopsychiatry*, (04),**29**(1996)127-134.
- Mittal S., Shah A.K., Barkmeier D.T. and Loeb J.A., "Systems Biology of Human Epilepsy Applied to Patients with Brain Tumors," *Epilepsia*, (s9),**54**(2013)35-39.
- Murali Dhar T., Nagarathnam D., Marzabadi M.R., Lagu B., Wong W.C., Chiu G., Tyagarajan S., Miao S.W., Zhang F. and Sun W., "Design and Synthesis of Novel α 1a Adrenoceptor-Selective Antagonists. 2. Approaches to Eliminate Opioid Agonist Metabolites via Modification of Linker and 4-methoxycarbonyl-4-phenylpiperidine Moiety," *Journal of Medicinal Chemistry*, (23),**42**(1999)4778-4793.
- Naegel S. and Obermann M., "Topiramate in the Prevention and Treatment of Migraine: Efficacy, Safety and Patient Preference," *Neuropsychiatric Disease and Treatment*, **6**(2010)17.
- Nakache R., Touil T., El Hessni A., Ouichou A., Bahbiti Y., Berkiks I., Chakit M. and Mesfioui A., "In vivo Acute Toxicity Assessment of a Novel Quinoxalinone (6-nitro-2 (1H)-quinoxalinone) in Wistar Rats", *Cogent Chemistry*, (1),**3**(2017), 1-11.
- Nakken K.O., "Adverse Metabolic Effects of Antiepileptic Drug Treatment", Novel Treatment of Epilepsy, InTech, Rijeka, 2011.

- Nielsen E.B., Suzdak P.D., Andersen K.E., Knutsen L.J., Sonnewald U. and Braestrup C., "Characterization of Tiagabine (NO-328), a New Potent and Selective GABA Uptake Inhibitor," *European Journal of Pharmacology*, (3),**196**(1991)257-266.
- Nonaka S., Katsube N. and Chuang D.-M., "Lithium Protects Rat Cerebellar Granule Cells Against Apoptosis Induced by Anticonvulsants, Phenytoin and Carbamazepine," *Journal of Pharmacology and Experimental Therapeutics*, (1),**286**(1998)539-547.
- Olianas M.C. and Onali P., "GABAB Receptor-Mediated Stimulation of Adenylyl Cyclase Activity in Membranes of Rat Olfactory Bulb," *British Journal of Pharmacology*, (3),**126**(1999)657-664.
- Özkanlı F., Gueney A., Çalış Ü. and Uzbay T., "Synthesis and Anticonvulsant Activity of Some New Dioxolane Derivatives," *Arzneimittelforschung*, (11),**53**(2003)758-762.
- Pajouhesh H. and Lenz G.R., "Medicinal Chemical Properties of Successful Central Nervous System Drugs," *NeuroRx*, (4),**2**(2005)541-553.
- Park S.P. and Kwon S.H., "Cognitive Effects of Antiepileptic Drugs," *Journal of Clinical Neurology*, (3),**4**(2008)99-106.
- Patani G.A. and Lavoie E.J., "Bioisosterism: A Rational Approach in Drug Design," *Chemical Reviews*, (8),**96**(1996)3147-3176.
- Pavia M.R., Lobbstael S.J., Nugiel D., Mayhugh D.R., Gregor V.E., Taylor C.P., Schwarz R.D., Brahce L. and Vartanian M.G., "Structure-Activity Studies on Benzhydrol-Containing Nipecotnic Acid and Guvacine Derivatives as Potent, Orally-Active Inhibitors of GABA Uptake," *Journal of Medicinal Chemistry*, (22),**35**(1992)4238-4248.
- Perucca P. and Gilliam F.G., "Adverse Effects of Antiepileptic Drugs," *The Lancet Neurology*, (9),**11**(2012)792-802.
- Petersen E.N., "DMCM: a Potent Convulsive Benzodiazepine Receptor Ligand," *European Journal of Pharmacology*, (1-2),**94**(1983)117-124.

- Petrera M., Wein T., Allmendinger L., Sindelar M., Pabel J., Höfner G. and Wanner K.T., "Development of Highly Potent GAT1 Inhibitors: Synthesis of Nipecotic Acid Derivatives by Suzuki–Miyaura Cross-Coupling Reactions," *ChemMedChem*, (5),**11**(2016)519-538.
- Pfeiffer M., Draguhn A., Meierkord H. and Heinemann U., "Effects of γ -aminobutyric acid (GABA) Agonists and GABA Uptake Inhibitors on Pharmacosensitive and Pharmacoresistant Epileptiform Activity *in vitro*," *British Journal of Pharmacology*, (3),**119**(1996)569-577.
- Prescott L., "Tiagabine offers effective seizure control," *Inpharma Weekly*, (1),**1085**(1997)15-16.
- Quandt G., Höfner G. and Wanner K.T., "Synthesis and Evaluation of N-Substituted Nipecotic Acid Derivatives with an Unsymmetrical Bis-Aromatic Residue Attached to a Vinyl Ether Spacer as Potential GABA Uptake Inhibitors," *Bioorganic & Medicinal Chemistry*, (11),**21**(2013)3363-3378.
- Reddy D.S. and Volkmer R., "Neurocysticercosis as An Infectious Acquired Epilepsy Worldwide," *Seizure-European Journal of Epilepsy*, **52**(2017)176-181.
- Regulska M., Pomierny B., Basta-Kaim A., Starek A., Filip M., Lasoń W. and Budziszewska B., "Effects of Ethylene Glycol Ethers on Cell Viability in The Human Neuroblastoma SH-SY5Y cell line," *Pharmacological Reports*, (6),**62**(2010)1243-1249.
- Riss J., Cloyd J., Gates J. and Collins S., "Benzodiazepines in Epilepsy: Pharmacology And Pharmacokinetics," *Acta Neurologica Scandinavica*, (2),**118**(2008)69-86.
- Rogawski M.A., "Brivaracetam: a Rational Drug Discovery Success Story," *British Journal of Pharmacology*, (8),**154**(2008)1555-1557.
- Roth F.C. and Draguhn A., "GABA Metabolism and Transport: Effects on Synaptic Efficacy," *Neural Plasticity*, **2012**(2012)1-12.

- Rowley N.M., Madsen K.K., Schousboe A. and White H.S., "Glutamate and GABA Synthesis, Release, Transport and Metabolism as Targets for Seizure Control," *Neurochemistry International*, (4),**61**(2012)546-558.
- Sałat K., Podkowa A., Kowalczyk P., Kulig K., Dziubina A., Filipek B. and Librowski T., "Anticonvulsant Active Inhibitor of GABA Transporter Subtype 1, Tiagabine, with Activity in Mouse Models of Anxiety, Pain and Depression," *Pharmacological Reports*, (3),**67**(2015)465-472.
- Sałat K., Podkowa A., Malikowska N., Kern F., Pabel J., Wojcieszak E., Kulig K., Wanner K.T., Strach B. and Wyska E., "Novel, Highly Potent and *in vivo* Active Inhibitor of GABA Transporter Subtype 1 With Anticonvulsant, Anxiolytic, Antidepressant and Antinociceptive Properties," *Neuropharmacology*, **113**(2017)331-342.
- Schwenk J., Metz M., Zolles G., Turecek R., Fritzius T., Bildl W., Tarusawa E., Kulik A., Unger A. and Ivankova K., "Native GABA B Receptors are Heteromultimers With a Family of Auxiliary Subunits," *Nature*, (7295),**465**(2010)231.
- Scimemi A., "Structure, Function, And Plasticity of GABA Transporters," *Frontiers in Cellular Neuroscience*, **8**(2014)161.
- Sernagor E. and Grzywacz N.M., "Spontaneous Activity in Developing Turtle Retinal Ganglion Cells: Pharmacological Studies," *Journal of Neuroscience*, (10),**19**(1999)3874-3887.
- Shekh-Ahmad T., Bialer M. and Yavin E., "Synthesis and Anticonvulsant Evaluation of Dimethylethanolamine Analogues of Valproic Acid and its Tetramethylcyclopropyl Analogue," *Epilepsy Research*, (2-3),**98**(2012)238-246.
- Shidore M., Machhi J., Shingala K., Murumkar P., Sharma M.K., Agrawal N., Tripathi A., Parikh Z., Pillai P. and Yadav M.R., "Benzylpiperidine-Linked Diarylthiazoles as Potential Anti-Alzheimer's Agents: Synthesis and Biological Evaluation," *Journal of Medicinal Chemistry*, (12),**59**(2016)5823-5846.

- Shiotsuki H., Yoshimi K., Shimo Y., Funayama M., Takamatsu Y., Ikeda K., Takahashi R., Kitazawa S. and Hattori N., "A Rotarod Test for Evaluation of Motor Skill Learning," *Journal of Neuroscience Methods*, (2),**189**(2010)180-185.
- Shorvon S.D., Andermann F. and Guerrini R., *The Causes Of Epilepsy: Common and Uncommon Causes in Adults And Children*; Cambridge University Press, 2011.
- Shrivastava S., Uppadhyay R., Trivedi P. and Jain D., "Synthesis and Evaluation of Amino Acid Analogues of Valproic Acid," *Indian Drugs*, (11),**33**(1996)571-573.
- Siddiqui N. and Ahsan W., "Triazole Incorporated Thiazoles as a New Class of Anticonvulsants: Design, Synthesis And *in vivo* Screening", *European Journal of Medicinal Chemistry*, **45**(2010)1536-1543.
- Siegel G.J., *Basic Neurochemistry: Molecular, Cellular and Medical Aspects*, Lippincott-Raven, Philadelphia, 1999.
- Sigel E. and Steinmann M.E., "Structure, Function, and Modulation of GABAA Receptors," *Journal of Biological Chemistry*, (48),**287**(2012)40224-40231.
- Sills G.J., "The Mechanisms of Action of Gabapentin and Pregabalin," *Current Opinion in Pharmacology*, (1),**6**(2006)108-113.
- Singh R.B., Singh G.K., Chaturvedi K., Kumar D., Singh S.K. and Zaman M.K., "Design, Synthesis, Characterization, and Molecular Modeling Studies of Novel Oxadiazole Derivatives Of Nipecotic Acid as Potential Anticonvulsant and Antidepressant Agents," *Medicinal Chemistry Research*, (1),**27**(2018)137-152.
- Sinha A. and Bhaumik D.K., "Treatment Expenditure Pattern of Epileptic Patients: a Study From a Tertiary Care Hospital, Kolkata, India," *Neurology Research International*, **2014**(2014)1-6.
- Sirven J.I., "Epilepsy: a Spectrum Disorder," *Cold Spring Harbor Perspectives in Medicine*, (9),**5**(2015)a022848.

- Skovstrup S., Taboureau O., Bräuner-Osborne H. and Jørgensen F.S., "Homology Modelling of the GABA Transporter and Analysis of Tiagabine Binding," *ChemMedChem*, (7),**5**(2010)986-1000.
- Šunjić V., and Parnham, M. J., *Organic Synthesis in Drug Discovery and Development. Signposts to Chiral Drugs*. Springer, 2011.
- Sutor B. and Luhmann H.J., "Involvement of GABAB Receptors in Convulsant-Induced Epileptiform Activity in Rat Neocortex *in vitro*," *European Journal of Neuroscience*, (11),**10**(1998)3417-3427.
- Taylor C.P., Angelotti T. and Fauman E., "Pharmacology and Mechanism of Action of Pregabalin: The Calcium Channel $\alpha 2-\delta$ (alpha2-delta) Subunit as a Target for Antiepileptic Drug Discovery," *Epilepsy Research*, (2),**73**(2007)137-150.
- Taylor C.P., Vartanian M.G., Schwarz R.D., Rock D.M., Callahan M.J. and Davis M.D., "Pharmacology of Cl-966: A Potent GABA Uptake Inhibitor, *in vitro* and in Experimental Animals," *Drug Development Research*, (3),**21**(1990)195-215.
- Thorner C., "Isosterism and Molecular Modification in Drug Design," *Chemical Society Reviews*, (4),**8**(1979)563-580.
- Tolou-Ghamari, Z., Zare, M., Habibabadi, J. M. & Najafi, M.R., "Antiepileptic drugs: a Consideration of Clinical and Biochemical Outcome in Patients with Epilepsy", *International Journal of Preventive Medicine*, (Suppl2)**4**(2013), S330-S337.
- Treiman D.M., "GABAergic Mechanisms in Epilepsy," *Epilepsia*, (s3),**42**(2001)8-12.
- Ugale V.G. and Bari S.B., "Structural Exploration of Quinazolin-4 (3H)-ones as Anticonvulsants: Rational Design, Synthesis, Pharmacological Evaluation, and Molecular Docking Studies," *Archiv der Pharmazie*, (11),**349**(2016)864-880.
- Van Spronsen M. and Hoogenraad C.C., "Synapse Pathology in Psychiatric and Neurologic Disease," *Current Neurology and Neuroscience Reports*, (3),**10**(2010)207-214.

- Vezzani A., Balosso S. and Ravizza T., "The Role of Cytokines in the Pathophysiology of Epilepsy," *Brain Behavior and Immunity*, (6),**22**(2008)797-803.
- Vezzani A., Fujinami R.S., White H.S., Preux P.-M., Blümcke I., Sander J.W. and Löscher W., "Infections, Inflammation and Epilepsy," *Acta Neuropathologica*, (2),**131**(2016)211-234.
- Viegas-Junior C., Danuello A., da Silva Bolzani V., Barreiro E.J. and Fraga C.A.M., "Molecular Hybridization: a Useful Tool in the Design of New Drug Prototypes," *Current Medicinal Chemistry*, (17),**14**(2007)1829-1852.
- Viteva E. and Semerdjieva M., "Enacted Stigma Among Patients with Epilepsy and Intellectual Impairment," *Epilepsy & Behavior*, **42**(2015)66-70.
- Walker K.A., Wallach M.B. and Hirschfeld D.R., "1-(Naphthylalkyl)-1H-imidazole Derivatives, a New Class of Anticonvulsant Agents," *Journal of Medicinal Chemistry*, (1),**24**(1981)67-74.
- Wang K.H., Penmatsa A. and Gouaux E., "Neurotransmitter and Psychostimulant Recognition by the Dopamine Transporter," *Nature*, (7552),**521**(2015)322-327.
- Weaver D.F., Principles and Practice of Computer-Aided Drug Design as Applied to the Discovery of Antiepileptic Agents, *Computational Neuroscience in Epilepsy*, pp. 515-191, Elsevier, 2008.
- White H.S., Smith M.D. and Wilcox K.S., "Mechanisms of Action of Antiepileptic Drugs," *International Review of Neurobiology*, **81**(2007)85-110.
- Yaari Y., Selzer M.E. and Pincus J.H., "Phenytoin: Mechanisms of its Anticonvulsant Action," *Annals of Neurology*, (2),**20**(1986)171-184.
- Youn Y., Sung I.K. and Lee I.G., "The Role of Cytokines in Seizures: Interleukin (IL)-1 β , IL-1Ra, IL-8, and IL-10," *Korean Journal of Pediatrics*, (7),**56**(2013)271-274.

- Yunger L., Fowler P.J., Zarevics P. and Setler P., "Novel Inhibitors of Gamma-Aminobutyric Acid (GABA) Uptake: Anticonvulsant Actions in Rats And Mice," *Journal of Pharmacology and Experimental Therapeutics*, (1),**228**(1984)109-115.
- Zerroug A., Belaidi S., BenBrahim I., Sinha L. and Chtita S., "Virtual Screening in Drug-Likeness and Structure/Activity Relationship Of Pyridazine Derivatives as Anti-Alzheimer drugs," *Journal of King Saud University-Science*, 2018, Article in Press, doi.org/10.1016/j.jksus.2018.03.024.
- Zhang J., Zhang P., Liu X., Fang K. and Lin G., "Synthesis and Biological Evaluation of (R)-N-(diarylmethylthio/sulfinyl) Ethyl/Propyl-piperidine-3-carboxylic acid Hydrochlorides as Novel GABA Uptake Inhibitors," *Bioorganic & Medicinal Chemistry Letters*, (13),**17**(2007)3769-3773.
- Zhang J.G., Jiang C.S., Lin G.Q. and Wen R., "A New Synthesis of 4, 4-diaryl/diheteroaryl-3-Butenyl Derivatives of Nipecotic Acids as GABA Transporter Inhibitors," *Chinese Chemical Letters*, (9),**16**(2005)1205-1208.
- Zheng C., Yang K., Liu Q., Wang M.Y., Shen J., Vallés A.S., Lukas R.J., Barrantes F.J. and Wu J., "The Anticonvulsive Drug Lamotrigine Blocks Neuronal $\alpha 4\beta 2$ Nicotinic Acetylcholine Receptors," *Journal of Pharmacology and Experimental Therapeutics*, (2),**335**(2010)401-408.
- Zheng J., Wen R., Luo X., Lin G., Zhang J., Xu L., Guo L. and Jiang H., "Design, Synthesis, and Biological Evaluation of the N-diarylalkenyl-piperidinecarboxylic Acid Derivatives as GABA Uptake Inhibitors (I)," *Bioorganic & Medicinal Chemistry Letters*, (1),**16**(2006)225-227.