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# Improvement of drugs efficiency by mechanochemically obtained nano particulated delivery systems

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**Newest results of application areas and advantages of mechano chemical technology of drug modification are considered. The main approach for pharmacy is based on preparation of solid disperse systems of pharmaceutics substances with different auxiliaries oligo and polysaccharide, plant's saponins, synthetic polymers, amorphous silica substances. After dissolution in water they form supramolecular nanoscale formations such as inclusion complexes, micelles and nanoparticles which containing drug molecules as «guest-host» types. Noted processes provide sufficiently increase of solubility, bioavailability and pharmacology action (lowering of meaning doses in 2-100 folds) of drug. Examples of drugs investigated.**

## Recent Publications

1. A V Dushkin, K V Gaidul and I A Goldina (2012) Antimicrobial Activity of Mechanochemically Synthesized Composites of Antibiotics and

| Drugs | Excipients for systems of drug delivery | Physico-chemical mechanisms of delivery systems | Pharmacological Test Results |
|---|---|---|---|
| Tranquilizers – diazepines: sibazon, medazepam, azaleptin | lactose, cellulose, arabinogalactan, hydroxyethylstarch, pectin | amorphisation complexation | Increasing of bioavailability and reducing of doses up to the 10 times |
| Non-steroidal anti-inflammatory: acetylsalicylic acid, ibuprofen, indomethacin, phenylbutazone, analgin | metal carbonates, arabinogalactan, hydroxyethylstarch, pectin, glycyrrhizic acid | salt formation, ionization, complexation, inclusion into micelles | Enhancing the therapeutic effect, reducing mean doses up to 10 times, reducing of toxicity |
| hypertensive and anti-arrhythmic - nifedipine, warfarin, miodarone | arabinogalactan, glycyrrhizin acid | complexation, inclusion into micelles | Reducing of mean doses up to 10-100 times |
| Polyphenolic natural compounds –flavonoids: quercetin, dihydroquercetin, rutin; and curcumin | metal carbonates, arabinogalactan, fibregam, derivatives of glycyrrhizic acid | ionization, complexation, inclusion into micelles | Increasing of antioxidant and capillary protective effect in 3-10 folds, antitumor action |
| Immunosuppressive drugs: azathioprine, cyclosporine | hydroxyethylstarch | complexation | Reducing of mean doses up to 10 times,reducing toxicity |
| Antibiotics: cefuroxime, cefoxitin, cefotaxime, ceftazidime, cefepime, ceftazidime, ceftriaxone, fosfomycin | nanostructured silica | amorphisation, Sorption at the micro- and nanoparticles | Increasing of antimicrobial activity 2-20 times prolongation of the action |
| Anthelmintic: albendazole, phenbendazole, niclozamide, praziquantel | arabinogalactan, hydroxyethylstarch, polyvinilpirrolidone, derivatives of glycyrrhizic acid | complexation | Increasing activity, reduced mean doses up to 10 times, reduced toxicity |
| Statins: simvastatin, atorvastatin Ca | arabinogalactan, derivatives of glycyrrhizic acid | complexation, inclusion into micelles | Increasing of hypolipidemic action and stability during storage |

*There is a brief discussion of various mill designs for mechanochemistry and recommendations for their use.*

Nanostructured Silicon Dioxide. Doklady Biochemistry and Biophysics 443:61–63.

2. A V Dushkin, Yu S Chistyachenko and D A Komarov (2015) About the Mechanism of Membrane Permeability Enhancement by Substances in Their Intermolecular Complexes with Polysaccharide Arabinogalactan from Larches *Larix sibirica* and *Larix gmelinii*. Doklady Biochemistry and Biophysics 460:9–12.
3. Y S Chistyachenko, E S Meteleva and M Y Pakharukova (2015) Physicochemical and pharmacological study of the newly synthesized complex of albendazole and polysaccharide arabinogalactan from larch wood. Current Drug Delivery 12(5):477-490.
4. Y S Chistyachenko, A V Dushkin and N E Polyakov (2015) Polysaccharide arabinogalactan from larch *Larix sibirica* as carrier for molecules of salicylic and acetylsalicylic acid: preparation, physicochemical and pharmacological study. Drug Delivery 22(3):400–407.
5. M V Khvostov, T G Tolstikova and S A Borisov (2016) Improving the Efficiency and Safety of Aspirin by Complexation with the Natural Polysaccharide Arabinogalactan Current Drug Delivery 13(4):582-589.
6. R Kong, E S Meteleva and Yu S Chistyachenko (2017) Enhanced solubility and bioavailability of simvastatin mechanochemically obtained complexes. International journal of pharmaceutics 534(1-2):108-118.
7. M V Khvostov, S A Borisov, T G Tolstikova and A V Dushkin (2017) Supramolecular Complex of Ibuprofen with Larch Polysaccharide Arabinogalactan: Studies on Bioavailability and Pharmacokinetics. European Journal of Drug Metabolism and Pharmacokinetics 42(3):431-440.
8. Q Zhang, N E Polyakov and Y S Chistyachenko (2018) Preparation of curcumin self-micelle solid dispersion with enhanced bioavailability and cytotoxic activity by mechanochemistry. Drug Delivery 25(1):198–209.

## Biography

Dushkin Alexandr Valerevich Educational background: 1972 – Novosibirsk State University, Department of Chemistry; 1977 - Ph.D; Institute of Chemical Kinetics and Combustion, Novosibirsk, Russia; 2006 -Doctor of chemical sciences, State University of Chemical Technology, Ivanovo, Russia; 2008-2018 – Professor, Correspondent member, Academician of Russia's Academy of Natural History. Institutional Affiliations: 1986 - present – Institute of Solid State Chemistry, Novosibirsk, Russia, Heading researcher, Head of scientific group. ~ 380 publications Research Interests: Supramolecular Chemistry, Mechanochemistry, Drug Delivery.

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