ACTIVE PHARMACEUTICAL SUBSTANCES – POSSIBILITIES AND EXPECTATIONS

B. Kratochvíl
University of Chemistry and Technology
Prague, Technická 5, 166 28 Praha 6, Czechia, bohumil.kratochvil@vscht.cz

Rational (Scientific) Medicine is based on treatment with chemical compounds (active pharmaceutical ingredients, APIs). APIs consist of either small or large active molecules. Medicines based on small molecules are called drugs, medicines containing large molecules are called biopharmaceuticals or biologics. There are about 12,500 APIs on the global pharmaceutical market, both drugs and biopharmaceuticals. APIs (in brand products) are ranked according to world sales every year.

The choice of the optimal API for a specific solid drug formulation means the optimization of its properties (solubility, dissolution rate, biavailability, stability, etc.) and patent non-collision statut, of course. For the selection of the optimal API, several dozens of solid pharmaceutical phases may be available from one active molecule (anhydrates, polymorphs, hydrates, salts, cocrystals). In pharmacy, the reduction in number of solid phases is given by the condition of pharmaceutical acceptability, see the GRAS directive [1].

The most widely used APIs in pharmaceutical formulations are salts and hydrated salts (over 50% of all current dosage forms). Salts are stable and well soluble in polar solvents (in an aqueous environment of the gastrointestinal tract, GIT), because they contain ionic bond. A necessary prerequisite for the formation of salts is the presence of ionizable groups (acidic or basic) in the molecule. In 75 % of the pharmaceutical salts, the active substance forms the cation in the 25 % anion. The most frequent counteranions are hydrochlorides, followed by sulphates and hydrobromides. The most frequent countercations are Na^+, Ca^{2+}, K^+ and Mg^{2+}. According the GRAS directive about 70 countercations and about 20 counteranions are available for salt formulations. Each pharmaceutical salt has a pHmax value with the maximum solubility, which can be correlated with the pH values of GIT parts for the best drug absorption.

The author thanks for the financial support of the grant GACR P206 16-10035S.

References

1. *https://www.fda.gov/Food/IngredientsPackagingLabeling/GRAS/.*

VIBRATIONAL SPECTROSCOPY – FROM MACRO- TO NANO-WORLD

Pavel Matějka[1], Martin Král[1], Alžběta Kokaislová[1], Marcela Dendisová[1], Marie Švecová[2], Adéla Jeništová[1], Jiří Janoušek[2]

[1]University of Chemistry and Technology
Faculty of Chemical Engineering, Department of Physical Chemistry
Technická 5, 166 28 Prague 6 - Dejvice, Czech Republic, pavel.matejka@vscht.cz

[2]University of Chemistry and Technology
Faculty of Chemical Engineering, Department of Analytical Chemistry
Technická 5, 166 28 Prague 6 - Dejvice, Czech Republic, marie.svecova@vscht.cz

Vibrational spectroscopy (VS) is represented by two complementary techniques based on either Raman scattering or infrared radiation absorption effect. Their surfaced-enhanced (SEVS) techniques are valuable tools for physico-chemical studies of the metal-adsorbate interface and for analytical applications focused on detection of low/trace amounts of various substances. Nevertheless, their disadvantage is inadequate lateral resolution which is equal to the lateral resolution of corresponding "normal" ("macro" and classical "micro") Raman and infrared spectroscopy limited by light diffraction. The irradiated surface area in usual SEVS micro-spectroscopic experiment contains relatively huge quantities of adsorbed molecules. However, for exact description of adsorption processes and intermolecular interactions, it is necessary to obtain spectra of single molecules and/or assemblies

of several molecules, and thus the information obtained by classic SEVS methods is insufficient.

Techniques that offer the best lateral resolution are those integrating SEVS spectroscopic techniques in the form of near-field techniques with scanning probe microscopy (SPM), especially atomic force microscopy (AFM). The most important ones are tip-enhanced Raman spectroscopy (TERS) and scanning near-field infrared microscopy (SNIM). TERS combines SPM with Raman spectroscopy and enables both outstanding detection sensitivity down to single-molecule level and high spatial resolution down to sub-nanometers. Thus, TERS provides chemical information and morphological description about the nano-scaled surface simultaneously. The tips used in TERS are silver/gold or silver/gold-coated materials. The apex is usually only a few atoms wide, which makes it the dominant enhancing source of Raman signals. The electromagnetic field, arising in the close proximity of the tip apex on which the laser beam is focused, gives rise to the signal of molecules or even one molecule in this (near) field. The reliability of TERS results relies essentially on the stability and reproducibility of the TERS tips. In the case of SNIM, the source of irradiation is a tunable IR laser, adjusted to a specific wavenumber for an imaging/mapping experiment. The laser beam is focused to a space under the tip and coupled with tip oscillations. SNIM measurement reveals the chemical nano-scaled imaging information on the sample based on "distribution" of absorption and radiation phase shifts at the selected wavenumber for the molecules which absorb the radiation at this wavenumber and are located in the gap between the tip and supporting surface/substrate.

The experiences related to the TERS and SNIM studies performed on various model samples focused on either nanomaterial development (including electrochemical sensors) or chemico-structural analysis of biologically relevant samples will be overviewed and discussed in this contribution.

Financial support from the UCT Prague is gratefully acknowledged.

DESIGN OF ROBUST NI-BASED CATALYSTS AND THE APPLICATION OF AN INTENSIFIED PROCESS FOR CO_2 DRY REFORMING OF METHANE TO SYNGAS

Zheng Jiang, Anatoliy Vorobev

Faculty of Engineering and the environment
University of Southampton, Southampton, SO17 1BJ, UK

CO_2 dry reforming of methane (DRM) to syngas (global demand achieved ~290 GW thermal/Annum in 2016) has recently gained ever-increasing attention for its great potential in converting two greenhouse gases into valuable syngas-a building block for the production of synthetic fuels, ferti lisers and chemicals. DRM can also be valorizing natural gas fields and aerobic digestion of bio-wastes with high concentration of CO_2, whose application is currently economically unprofitable. However, the DRM suffers from grand challenges in catalysts deactivation due to sintering and coking. which stimulate the exploration of stable yet robust catalytic materials and intensified reforming processes.

Addressing the above challenges facing DRM, we dedicate improving the performance of cost-effective Ni-based catalysts via tailoring redox property and metal-support interaction, in which the combination of inelastic neutron scattering and