Study of the Influence of Silver or Gold Nanoparticles on the Drug Penetration Using Vibrational Spectroscopy

UCT PRAGUE

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Introduction

In this study pig skin (PS) was used as a model of human skin to investigate interaction between skin layers and basic ointment with different proportion of AgNPs or AuNPs.

AgNPs/AuNPs added to the basic ointment (BO) can play two possible roles. Firstly, they can enhance the IR spectra known as SEIRA (Surface-enhanced Infrared Absorption) or Raman spectra known as SERS (Surface-Enhanced Raman Scattering). Secondly, this NPs can affect the penetration properties of pig skin.

ATR-FTIR (Fourier-Transform InfraRed Attenuated Total Reflectance) technique and **FT-Raman spectrometry** were used successfully to study penetration of pharmaceuticals including time-dependent spectral measurements and their chemometric evaluation.

Instrument Settings

IR spectrometer

ATR-FTIR: resolution 4 cm^{-1}, 2 hours of measurements (25 spectra in 1 sequence)

Compensation (air humidity, CO_2 and H_2O from dispersion of NPs)

Raman spectrometer

Nd:YAG (1064 nm), resolution 4 cm^{-1}, 2 hours of measurement (32 spectra in 1 set)

Experimental

Preparation of Silver and Gold Nanoparticles in aqueous medium

a) Reduction by sodium citrate

$$AgNO_3 + Na_3C_6H_5O_7 \xrightarrow{100^{\circ}C} Ag(c)\ (45\ nm)$$

$$KAuCl_4 + Na_3C_6H_5O_7 \xrightarrow{100^{\circ}C} Au(c)\ (15\ nm)$$

b) Reduction by sodium borohydride

$$AgNO_3 + NaBH_4 \xrightarrow{0^{\circ}C} Ag(b)\ (15\ nm)$$

c) „Green" synthesis of AgNPs and AuNPs

- reduction by D-Glucose (D-Glu), Amylose, Ascorbic acid (AA), Gelatin, Honey, Kiwi juice

Preparation of ointments

Centrifuged NPs were mixed into the BO in several mass fractions, i.e., 1:1, 1:3 or 1:5. Individually prepared NPs-modified ointments were then applied on the uppermost layer of pig skin. We have tested also penetration of two water-soluble vitamins (pyridoxine and thiamine) added to the BO and BO modified by NPs.

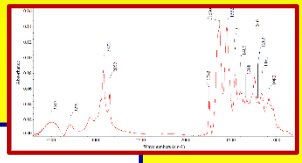
Multivariate analytical methods

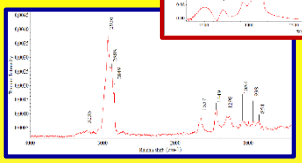
Hundreds of spectra were analyzed by SIMCA (Soft Independent Modelling of Class Analogy), PCA (Principal Component Analysis) and PLS (Partial Least Squares) regression.

Results

• IR and Raman spectrum of untreated PS

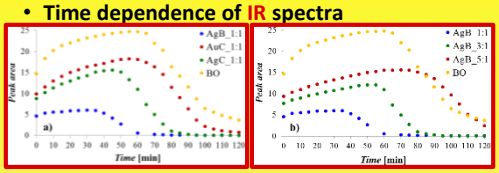
Raman: Strong vibrational bands of saturated aliphatic skeletons





IR: Strong vibrational bands of amides, saturated aliphatic skeletons, esters and OH-components

• Time dependence of IR spectra



a) different **types** of NPs in basic ointment (BO)

b) different **quantity** of NPs in basic ointment (BO)

- The *first part* is represented by an evident **increase** of peak areas
- The *second part* is described by the strong **decrease** of peak areas and represents the main process of penetration
- The *third part* is the end of penetration

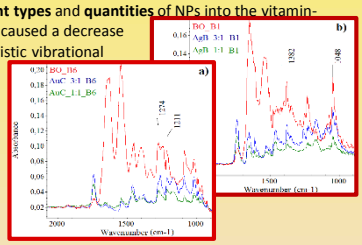
It is evident that not only **different types** of NPs but also their actual **quantities influence a penetration rate**.

• Pyridoxine and Thiamine penetration

Additions of **different types** and **quantities** of NPs into the vitamin-modified ointments caused a decrease of marked characteristic vibrational bands of

a) Pyridoxine 1274 and 1211 cm^{-1}

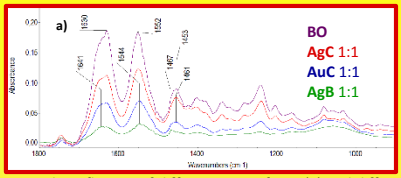
b) Thiamine 1382 and 1048 cm^{-1}

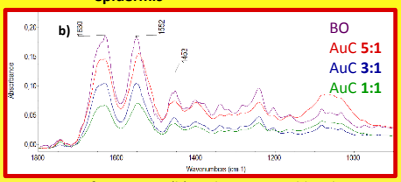


• Spectral shifts of characteristic IR vibrational bands due to NPs addition to BO: 8 – 17 cm^{-1}

Band positions of BO [cm^{-1}]		Standard reduction [cm^{-1}]			„Green" synthesis [cm^{-1}]
		AgB_1:1	AgB_3:1	AuC_3:1	
1630	ν(CO) - amide I	1641	1640	/	1647
1552	δ(NH) - amide II	1544	1543	/	1542
1453	$\delta(CH_2)$	1467	/	1461	1464

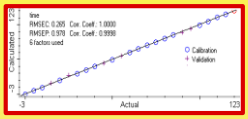
- No position changes of vibrational bands of untreated PS against BO-treated PS were observed
- Spectral shifts are observable for amide I and II bands and $\delta(CH_2)$ vibration especially for AgB 1:1, AgB 3:1, AuC 3:1 and all NPs prepared by „green" synthesis
- **Spectral shifts result from NPs interactions with lipid and keratin components in epidermis**





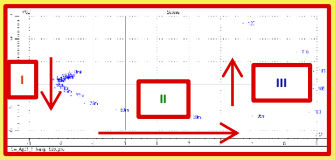
- The influence of different type of NPs (a) and different quantity of same NPs (b) is characterized by changes of spectral intensities. The main **decreases** were observed for spectral bands of **saturated aliphatic skeletons**, **OH-components**, **esters**, and furthermore for **amides**.

• Statistical evaluation of IR and Raman spectra



PLS regression

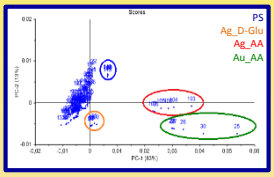
Time prediction is possible for all prepared NPs.



This three parts correspond to graphs of time dependence of band intensities.

Data organization along PCs

- The *first part* - data are situated along PC2
- The *second part* - the main part of penetration, differentiation of spectra
- The *third part* – the end of penetration



PCA of Raman spectra

Only Raman spectra of untreated PS and spectra of PS treated by BO with AuNPs reduced by AA and AgNPs reduced by D-Glu and/or AA were differentiated. The rest of spectra are situated almost along PC2.

Conclusion and our Future Plans

- NPs **do not enhance** noticeably **IR** and **Raman signals** in the case of untreated and/or treated PS
- **Interactions** of NPs-modified BO with **lipid and keratin** components of epidermis were observed
- The use of NPs as possible **penetration enhancers**
- Possibility of **time prediction** of spectral data
- Observation of the **three main stages of penetration process** of substances through skin surface

For better understanding we plan more testing by

- **Near Field IR microspectrometry**
- **Raman microspectrometry**

Acknowledgement

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