IR, RAMAN, SERS AND DFT STUDY OF PINDOLOL AND VERAPAMIL DRUGS

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Abstract

IR, Raman and surface-enhanced Raman scattering (SERS) spectra of protonated molecular forms of pindolol (PIN) and verapamil (VER) were recorded, and the vibrational bands assigned by means of density functional theory (DFT) based calculations. The adsorption geometry to the silver surface of the investigated drugs was derived by considering the molecular electrostatic potential (MEP) and the SERS surface selection rules. Both molecules are adsorbed through the oxygen atoms and π-electrons of the rings to the silver surface. The whole structure of the molecules lies on the metal surface with the aromatic rings in a flat(tilted) and bent position for PIN and VER, respectively.

Pindolol (PIN) is a nonselective beta blocker with partial beta-adrenergic receptor agonist activity. In high doses it increases pulse rate, blood pressure and bronchodilation. It also has membrane stabilizing and antiarrhythmic effects.

Verapamil (VER) is an L-type calcium channel blocker of the phenylalkylamine class. It has been used in the treatment of hypertension, angina pectoris, cardiac arrhythmia, and most recently, cluster headaches. It is also an effective preventive medication for migraine. It is more effective than digoxin in controlling ventricular rate.

Key words: IR, Raman, SERS, DFT, pindolol, verapamil.

Experimental techniques

FT-IR

powder samples, room temperature,
Bruker Equinox 55 FT-IR spectrometer, ZnSe ATR, DTGS detector

FT-Raman

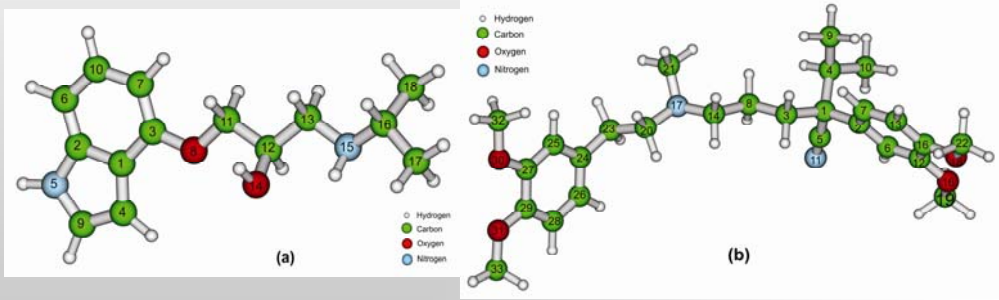
backscattering geometry, Bruker FRA 106/S Raman accessory, 1064 nm Nd:YAg laser, 400 mW
resolution 2 cm^{-1}

SERS

Advantage 532 spectrometer (DeltaNu USA). 532 nm frequency doubled NdYAG laser,
40 mW, resolution ~8 cm^{-1}
For SERS measurements 50 µl of analyte were added to 0.5 ml silver colloid. The silver colloidal SERS substrate, was prepared by reducing Ag^+ with hydroxylamine. Briefly, 0.017 g silver nitrate were solved in 90 ml distilled water. In a separate recipient, 0.011 g of hydroxylamine hydrochloridewere solved in 10 ml water, followed by the addition of 0.1 ml sodium hydroxide solution, 2 mol/l (v). The hydroxylamine / sodium hydroxide solution was then added rapidly to the silver nitrate solution under vigorous stirring. After a few seconds a grey brown colloidal solution resulted, with pH value 9, and was further stirred for 10 minutes.

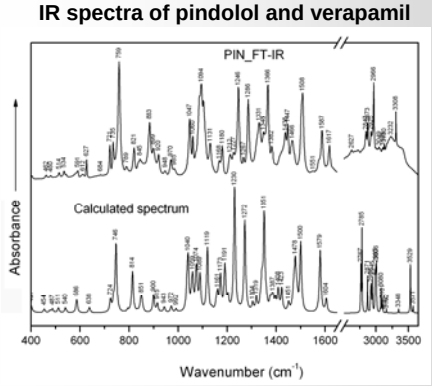
Computational methods

DFT exchange-correlation functionals: B3LYP & BLYP, basis sets: "spectroscopic" 6-31G(d)



Molecular structure of pindolol (a) and verapamil (b).

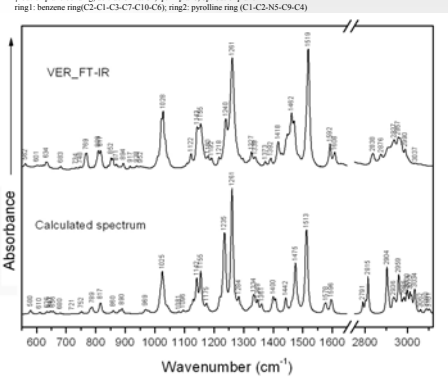
IR spectra of pindolol and verapamil



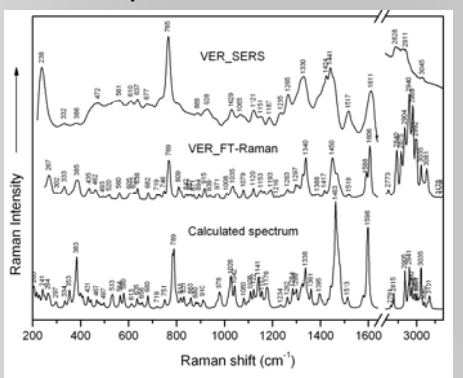
Selected experimental FT-IR bands and calculated wavenumbers of PIN.

Experimental wavenumbers (cm^{-1}) FT-IR	Calculated wavenumbers (cm^{-1}) B3LYP	Band assignment
591	586	ip. ring1 deformation+δ(CH_2)+δ(CH)
627	638	ip. ring1, ring2 deformation+δ(CH_2)+δ(CH)
721	724	op. CH ring1,CH ring2 bending
759	746	op. CH ring1,CH ring2 bending
821	814	δ(N15H)+δ(CH_3)
883	900	δ(CH_2)+δ(CH_3)+δ(CH)+δ(N15H)
1047	1040	δ(CH ring2)+δ(CH_2)+δ(CH_3)+δ(CO)+ν(CC)
1060	1059	δ(CH ring2)+δ(N5H)+δ(CH_2)+δ(CH_3)
1094	1089	δ(CO14H)+ν(CC)+ν(C12O)++δ(CH) +δ(CH_2)+δ(CH_3)+δ(N15H)
1131	1119	δ(CH ring2,ring1)+δ(N5H)+ν(C11O8)
1180	1173	ν(C16N15)+ρ(CH_3)+ρ(CH_2)
1246	1230	δ(CH ring2,ring1)+δ(N5H)+ν(C3O8)+ip. ring1, ring2 deformation
1286	1272	δ(CH ring2,ring1)+δ(N5H)+ν(C3O8)+ip. ring1, ring2 deformation
1366	1351	ip. ring1, ring2 deformation+δ(CH ring2,ring1)+δ(N5H)+ν(C3O8C11)
1466	1478	δ(CH_2)+δ(CH_3)+δ(N15H)
1508	1500	ν(CC ring1, ring2)+δ(CH ring1, ring2)+δ(N5H)+δ($C11H_2$)
1587	1579	ν(CC ring1, ring2)+δ(CH ring1, ring2)+δ(N5H)+δ($C11H_2$)
1617	1604	ν(CC ring1, ring2)+δ(CH ring1, ring2)+δ(N5H)
2873	2871	$ν_s$($C11H_2$)
2966	2945	$ν_{as}$($C13H_2$,$C11H_2$)
3308	3348	ν(N15H)

ν- stretch, $ν_s$- symmetric stretch, $ν_{as}$- asymmetric stretch, δ- in plane bending, ρ- rocking, γ-out-of-plane bending, def.-deformation, ip.-in plane, op. -out of plane
ring1: benzene ring(C2-C1-C3-C7-C10-C6); ring2: pyrolline ring (C1-C2-N5-C9-C4)



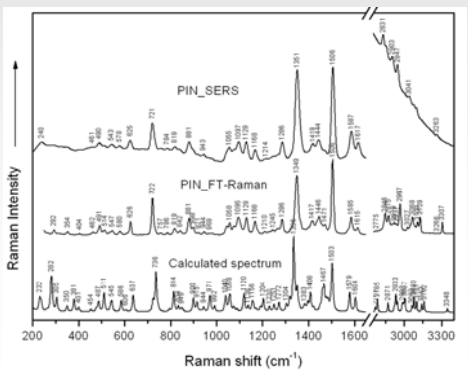
SERS, FT-Raman and calculated spectra of VER and PIN

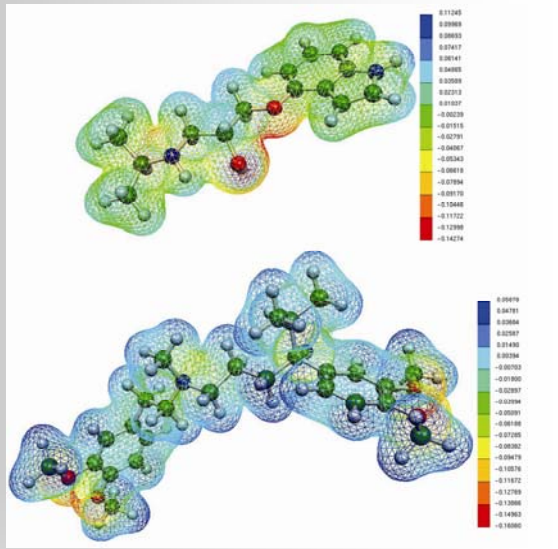


Selected experimental SERS, FT-Raman bands and calculated wavenumbers of VER.

Experimental wavenumbers (cm^{-1}) SERS	FT-Raman	Calculated wavenumbers (cm^{-1}) B3LYP	Band assignment
238	267	264	ρ(CH_3)
378	385	383	δ(O31CH_3, O30CH_3, O16CH_3, O18CH_3, CH_3)
765	769	789	ν(CC ring1)+ip. ring1 deformation+δ(CH ring1)+ δ(CH_2)+ ν(C12O16, C15O18)
1029	1035	1026	ν(CC ring1)+ν(O16CH_3, O18CH_3)
1330	1340	1338	δ(CH_2)+ρ(CH_2)+ν(CC ring1)
1441	1450	1463	δ(CH_3)+δ(CH_2)
1517	1519	1513	ν(CC ring1)+δ(CH ring1)+ν(C12O,C15O) δ(O16CH_3, O18CH_3)+δ(CH_3)
1611	1606	1598	ν(CC ring2)+δ(CH ring2)
2826	2840	2815	ν(C20H54,C14H49,C21H56)
2911	2940	2941	$ν_s$(C10H_3,C9H_3,C3H_3,C8H_3)
3045	3035	3035	$ν_{as}$(C32H_3,C33H_3)

ν- stretch, $ν_s$- symmetric stretch, $ν_{as}$- asymmetric stretch, δ- in plane bending, ρ- rocking, γ-out-of-plane bending, def.-deformation, ip.-in plane, op. -out of plane
ring1: benzene ring(C2-C6-C12-C15-C13-C7); ring2: benzene ring(C24-C29)





B3LYP/6-31G(d) calculated 3D electrostatic potential contour map of PIN (top) and VER (bottom), in atomic units.

Conclusions

The recorded IR, Raman and SERS spectra of PIN and VER were assigned based on the DFT theoretically calculated spectra.

Based on the MEP maps which show the most electronegative sites of these molecules and SERS selection rules the adsorption of PIN and VER on silver monoparticles was shown to occur by the oxygen atoms and the ring π-electrons.

The whole structure of PIN and VER lies on the silver surface with a flat and bent orientation.

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