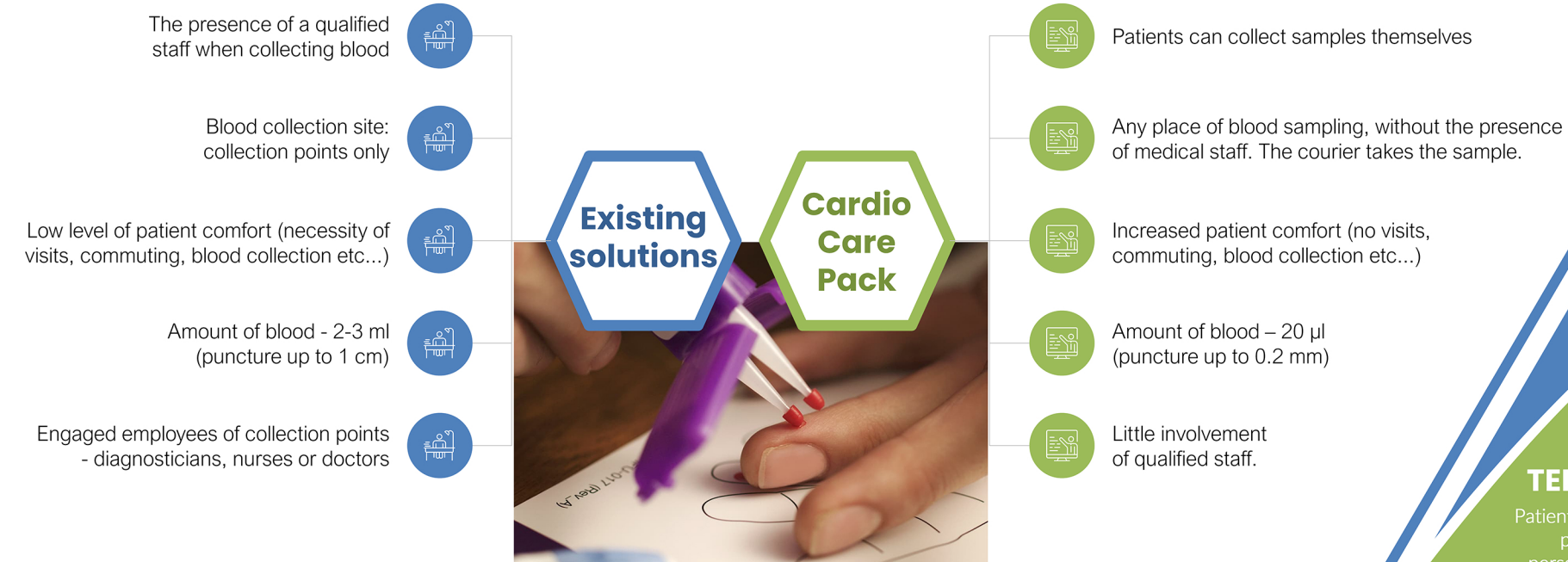


CardioCarePack – personalized medicine system to improve live quality of patients suffering from cardiac arrhythmias.

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Cardiac arrhythmia affects approximately 12.6% of people over the age of 65. Ventricular arrhythmias are considered as responsible for 75% to 80% of sudden cardiac deaths. Drug therapy monitoring (TDM) in Anti-Arrhythmic Drugs (AAD) is essential for patient management when their have narrow therapeutic range, their use is associated with several serious adverse drug reactions, has a long, multiphasic elimination of up to several dozen days or formation of active metabolites with the action distinct form the parent drug. Developed assay named “CardioCarePack” is based on the use of capillary blood collected at home by a patient with volumetric absorptive microsampling (VAMS), quantitative analysis of selected drugs and their metabolites and a telemedical system that integrates all data between a doctor, patient and laboratory supporting the therapy process.

One of the key features of CardioCarePack is the ability for patients to collect samples on their own.



All the tested compounds were separated using reversed-phase chromatography and analyzed using QTRAP 5500+ LC-MS/MS system (SCIEX) operating in positive MRM mode. The MS/MS scanning was divided into 5 periods (Fig. 2) in which the ion source parameters were adjusted to increase the sensitivity for compounds that exhibit poor ionization. For Digoxin period Q1 resolution was set to “low”. Data processing and quantitation analysis were performed using SCIEX OS software.

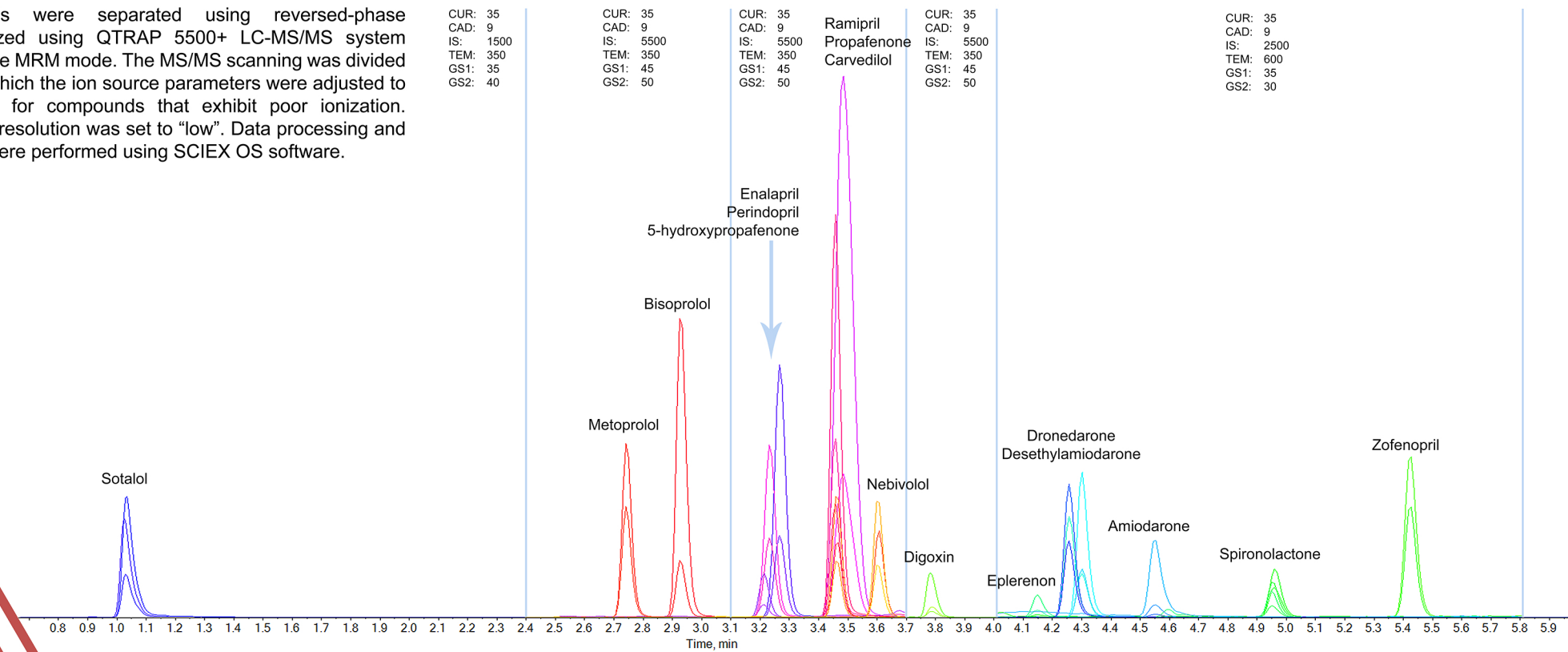


Fig. 2. XIC chromatogram of the selected compounds with periods and ions source settings applied.

Tab. 1. Summarized data for anti-arrhythmic TDM with samples collected by VAMS.

Analyte	Therapeutic index [µg/L]	Working range [µg/L]	LLOQ		Serum to Mitra ratio*	
			[µg/L]	Signal to Noise	S/M ratio	%CV
Sotalol	1400 - 1700	10 - 2500	< 10	3406	0.94	6.05
Metoprolol	3 - 270	1 - 250	< 1	261	0.87	10.81
Bisoprolol	3 - 50	2.5 - 250	< 1	438	1.06	4.35
5-OH Propafenone	153 - 337	50 - 2500	< 10	2677	1	7.33
Perindopril	80 - 150	10 - 250	< 1	811	1.86	4.91
Enalapril**	10 - 100	2.5 - 250	< 1	561	N/A	N/A
Propafenone	100 - 1000	1 - 250	< 1	1136	1.82	9.88
Ramipril	10 - 10000	2.5 - 250	< 1	435	1.15	7.90
Carvedilol	6.93 - 77	2.5 - 250	< 1	298	1.86	4.89
Digoxin	0.5 - 2	0.25 - 25	0.25	7	0.69	1.22
Nebivolol	0.5 - 1.5	0.25 - 25	0.1	6	1.04	1.71
Eplerenone	200 - 1700	10 - 2500	< 1	95	1.78	5.12
Spirinolactone	10 - 300	2.5 - 250	< 1	33	1.76	5.19
Dronedarone**	80 - 170	2.5 - 250	< 1	127	N/A	N/A
Desethylamiodarone	200 - 1000	10 - 2500	< 10	456	1.28	12.43
Zofenopril	50 - 170	2.5 - 250	< 1	57	2.38	34.43
Amiodarone	1000 - 2500	10 - 2500	< 10	438	2.1	17.45

* - S/M ratio is calculated on the basis of parallel analysis of serum and VAMS collected blood from patients in medical facility (four control tests every half a year during 2-years study)
 ** - no patients treated with this drugs during 2-years clinical study

The project involved more than 300 patients who had been monitored for 2 years during regular pharmacological therapy. Every half a year during a visit in medical facility venous blood for serum testing and capillary blood on the Mitra® sorbent were collected. Between the visits patients were collecting samples by VAMS themselves at home. All samples were analyzed by fully validated procedure where among the others linearity ($r \geq 0.995$), accuracy (80 – 120%), reproducibility (%CV ≤ 15%) for both Mitra® and serum were calculated.

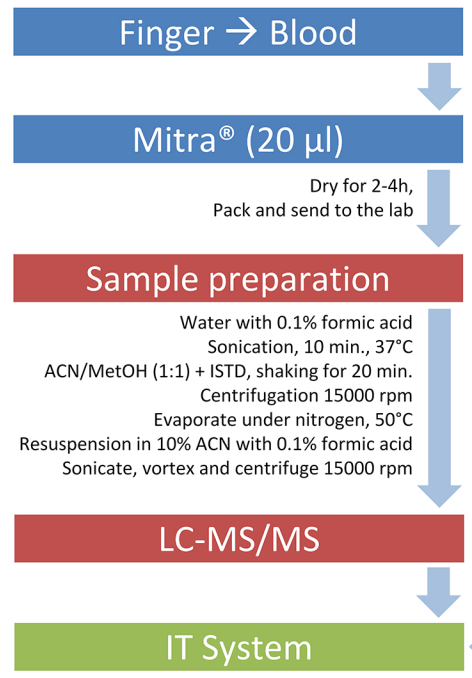
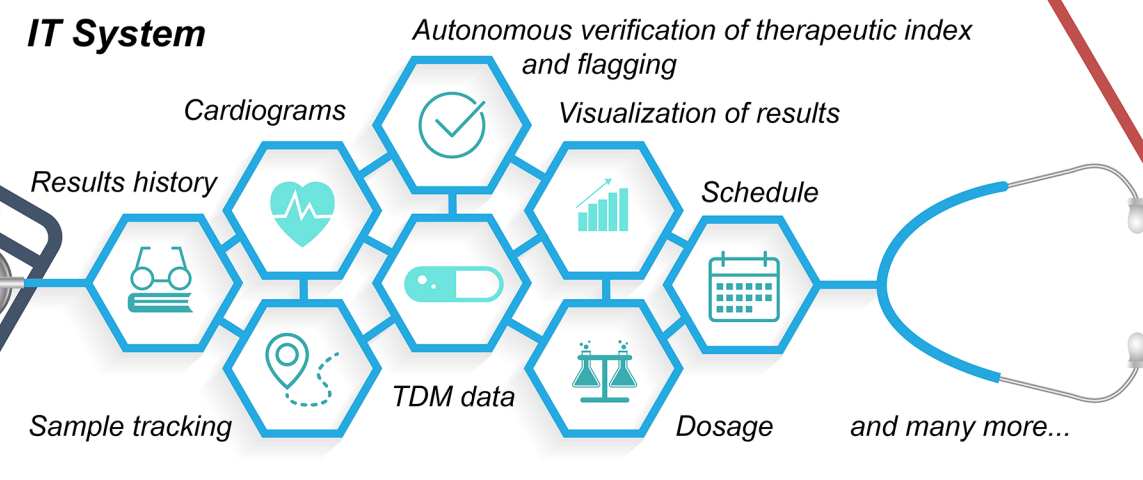
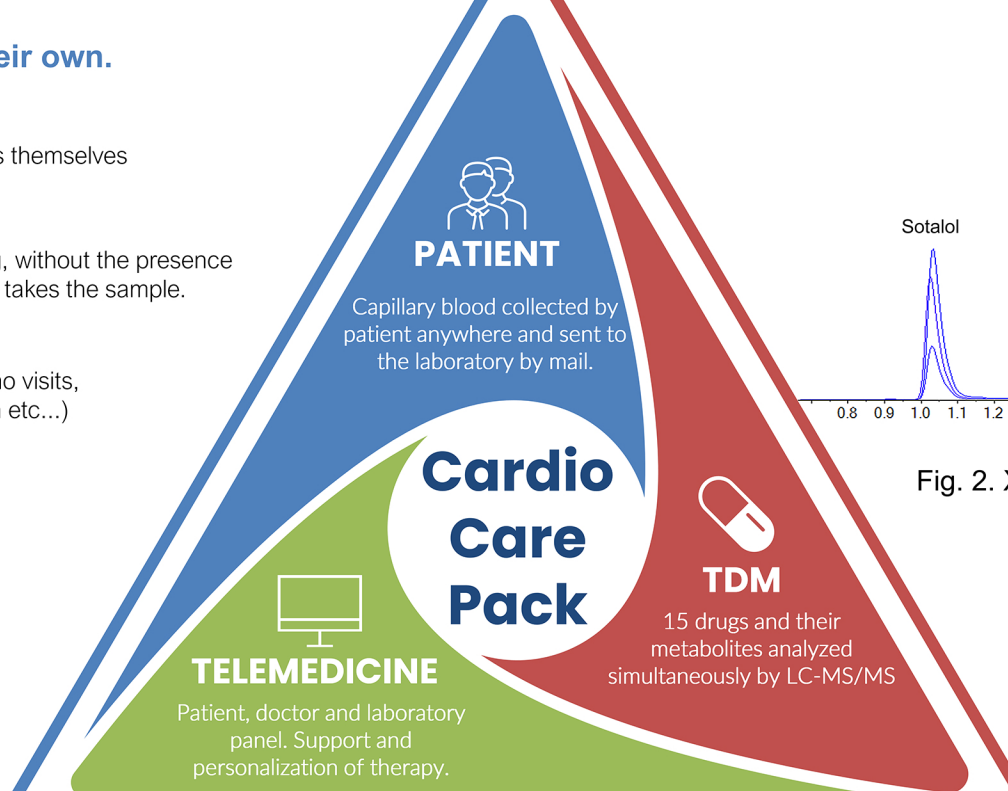


Fig. 1. CardioCarePack - how does it work?



“CardioCarePack support therapy and improves healthcare of patients suffering from cardiac arrhythmias on the basis of collected within the software data. It fits in with modern trends of home-based sample collection and personalized medicine”