Analysis of Biological Fluids

The AccuTOF-DART can detect a variety of substances in biological fluids such as urine, blood, and saliva with little or no sample preparation. These substances include drugs, amino acids, lipids, and metabolites.

Urine samples were analyzed by dipping a melting point tube in urine and placing the sample in front of the DART ion source. Figure 1 shows positive-ion DART mass spectra of a urine sample from a subject taking ranitidine to reduce stomach acid production. The enlarged view in the inset shows the ranitidine metabolites desmethyl ranitidine and ranitidine N-oxide.

Figure 2 shows a negative-ion DART mass spectrum of urine from the same subject. Compounds detected that fall within 0.002 u within the theoretical masses for compounds in a target list include nucleotide bases, caffeine metabolites, uric acid and related compounds, and organic acids.

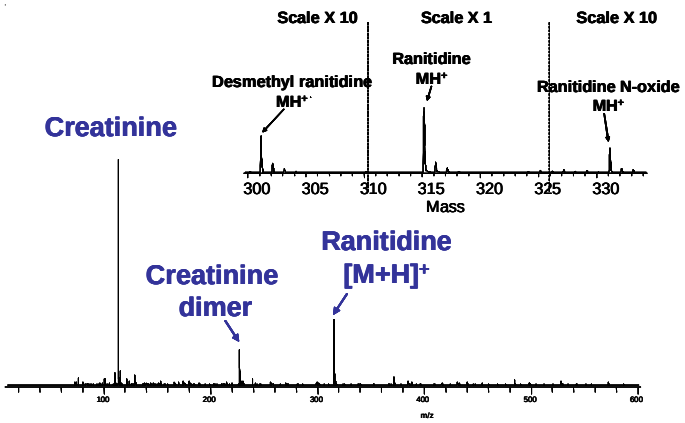

Figure 1. Ranitidine metabolites in human urine.

Name	Meas.	Calc.	Diff(u)	Rel. Abund.
GBL	85.0295	85.0290	0.0006	11.0317
Pyruvic_acid	87.0084	87.0082	0.0002	7.1700
Lactic_acid	89.0236	89.0239	-0.0002	8.3658
Cresol	107.0492	107.0497	-0.0004	0.9294
Creatinine	112.0513	112.0511	0.0002	81.6851
Purine	119.0354	119.0358	-0.0004	31.9510
Dihydro_methyluracil	127.0486	127.0508	-0.0021	23.3773
pGlu	128.0353	128.0348	0.0006	59.2337
Methylmaleic_acid	129.0212	129.0188	0.0024	37.1191
Me_succinate/diMe_malonate	131.0368	131.0358	0.0010	19.3593
Deoxyribose	133.0489	133.0501	-0.0012	28.3521
Hypoxanthine	135.0306	135.0307	-0.0001	100.0000
Methyl_hypoxanthine	149.0454	149.0463	-0.0009	37.5243
Hydroxymethyl_methyl_uracil	155.0453	155.0457	-0.0003	55.5832
Methylxanthine	165.0408	165.0412	-0.0004	32.4341
Hippuric_acid	178.0513	178.0504	0.0009	66.4487
Glucose	179.0552	179.0556	-0.0004	39.7499
Dimethylxanthine	179.0552	179.0569	-0.0017	39.7499
Dimethyluric_acid	195.0527	195.0518	0.0009	23.7577
AAMU (caffeine met.)	197.0667	197.0675	-0.0007	79.6617
Cinnamalidinemalonic_acid	217.0483	217.0501	-0.0017	60.5399
AFMU (caffeine met.)	225.0643	225.0624	0.0019	21.9092
Cytidine	242.0801	242.0777	0.0024	3.4545
Uridine	243.0641	243.0617	0.0024	21.1156
Phenylacetyl_glutamine	263.1033	263.1032	0.0001	48.9665
Ranitidine	313.1321	313.1334	-0.0013	8.7459
Ranitidine+Cl	349.1113	349.1101	0.0011	11.7296

Table I. Compounds identified by exact mass.

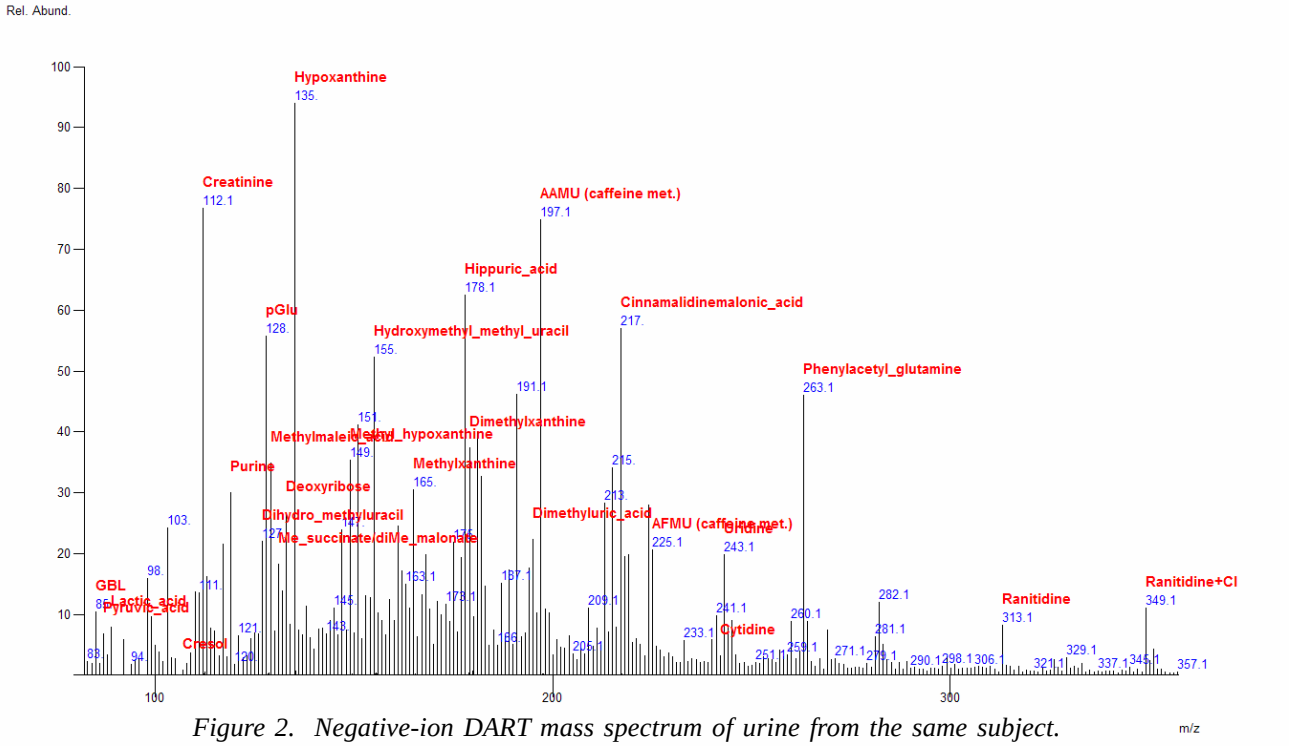

Figure 2. Negative-ion DART mass spectrum of urine from the same subject.

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Quantitative analysis is possible. DART response is proportional to sample quantity. However, the absolute response is dependent on the position of the sample in the DART gas stream and on position of the sample relative to the mass spectrometer sampling orifice.

Addition of an internal standard can compensate for variations in ion abundance due to differences in placement of the sample tube in the DART ion source. Figure 3 shows the working curve obtained for urine samples that have been spiked with gamma hydroxy butyrate (GHB) at concentrations ranging from 0 ppm to 800 ppm. Samples were spiked with 50 ppm of a deuterated internal standard (d6-GHB). A melting point tube was dipped into the urine samples and then placed in front of the DART source. Results were obtained within seconds. Five replicates were measured for each concentration over a period of five days. Excellent linearity was observed.

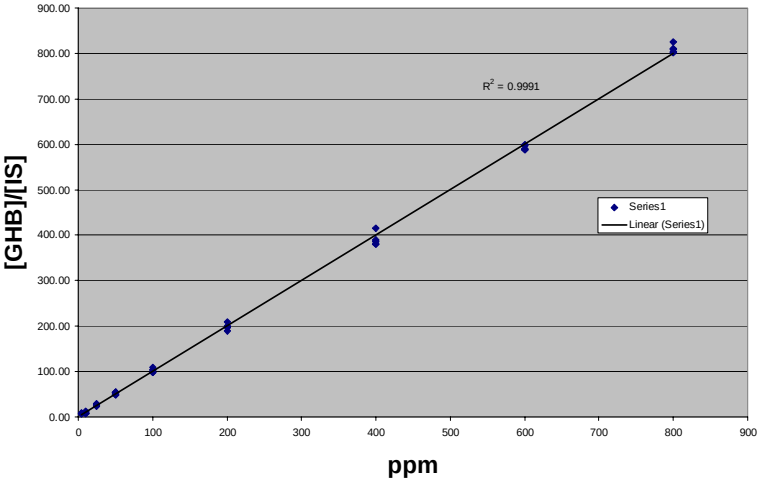

Figure 3. GHB in urine.

Although some compounds can be detected in whole blood, whole blood is not well suited for analysis with no sample preparation. Minimal sample preparation can reveal compounds that are not readily detected in whole blood. Figure 4 shows amino acids detected in whole blood. Centrifuging the blood sample to remove blood cells makes it possible to detect triglycerides (Figure 5). The addition of acetonitrile to remove blood proteins makes it possible to detect other compounds, such as ranitidine (Figure 6).

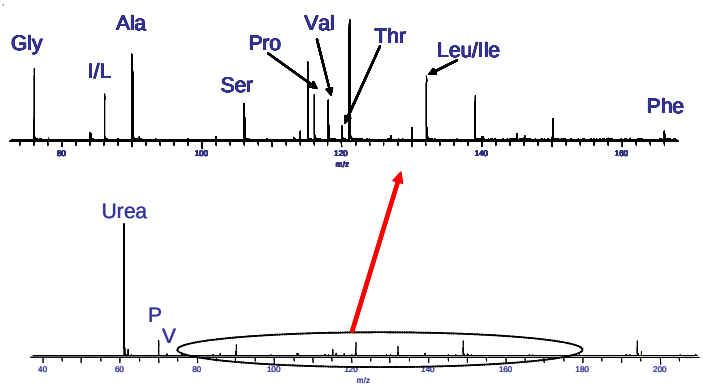

Figure 4. Amino acids in whole human blood.

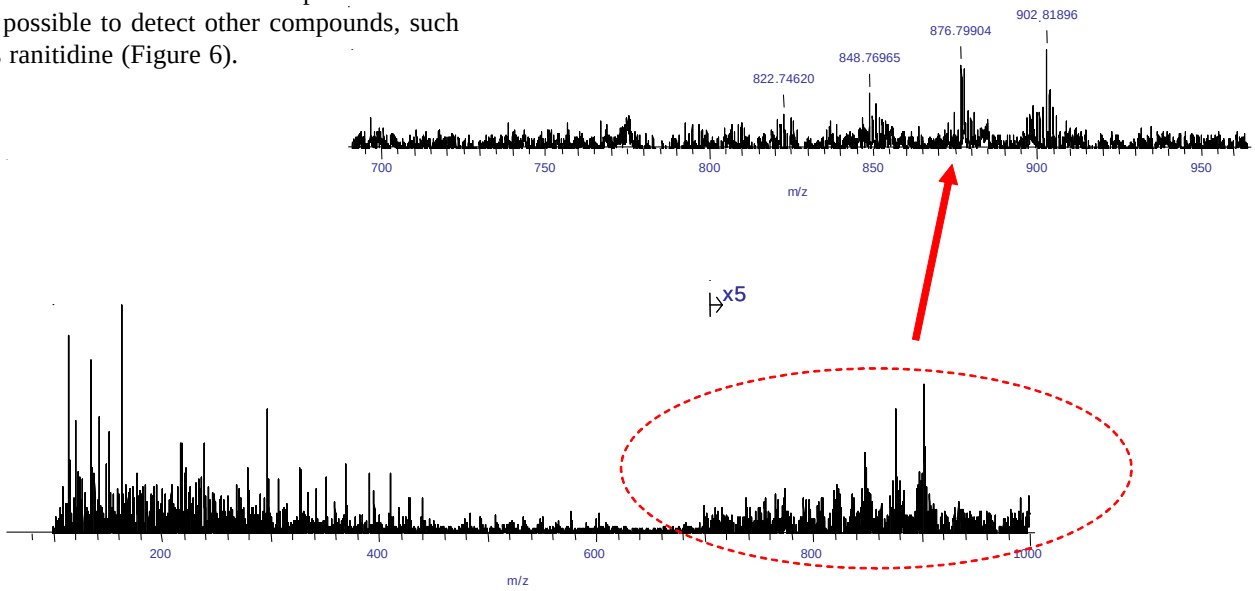

Figure 5. Triglycerides in human blood plasma.

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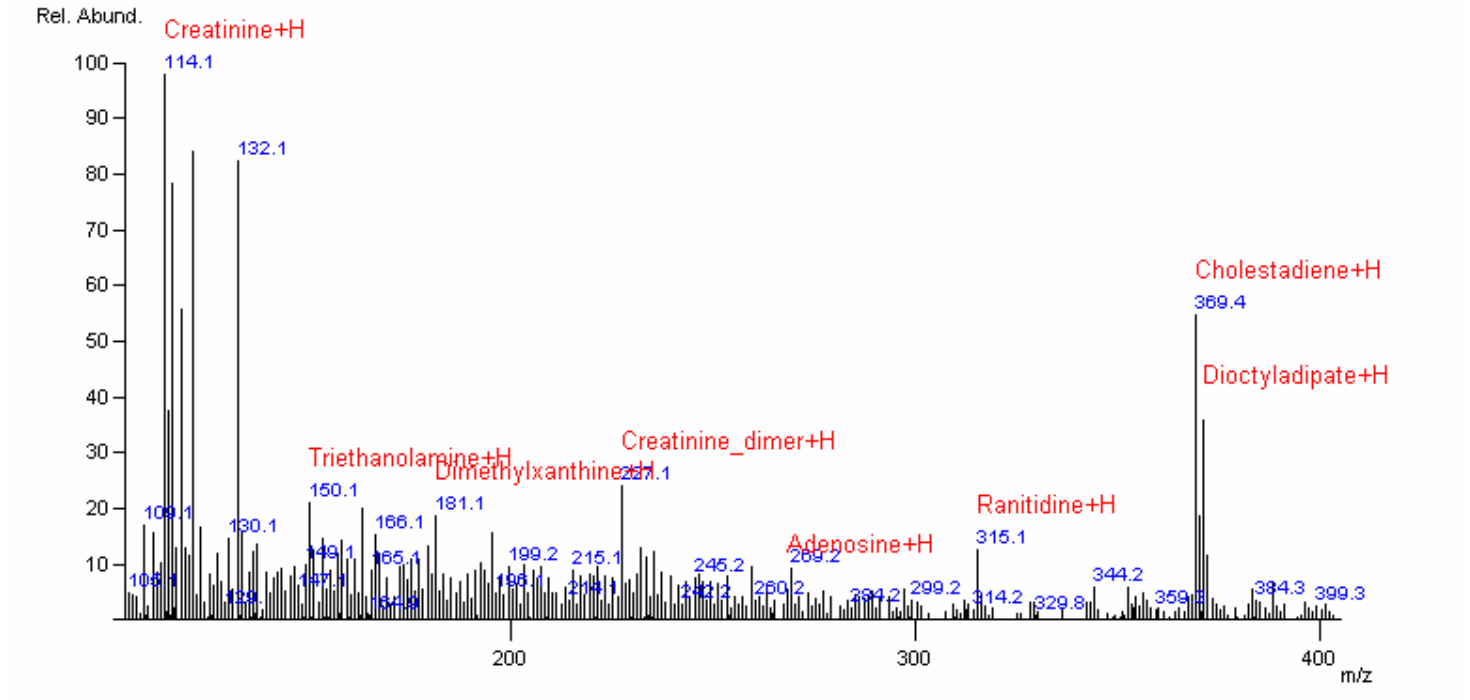

Figure 6. Compounds detected in human plasma after addition of acetonitrile. Amino acids A, P, V, L/I are detected, but not labeled in this figure. Note the presence of caffeine metabolites (dimethylxanthines). Triethanolamine is present in many consumer products and dioctyl adipate is a common plasticizer that may have been extracted from the plastic vial.

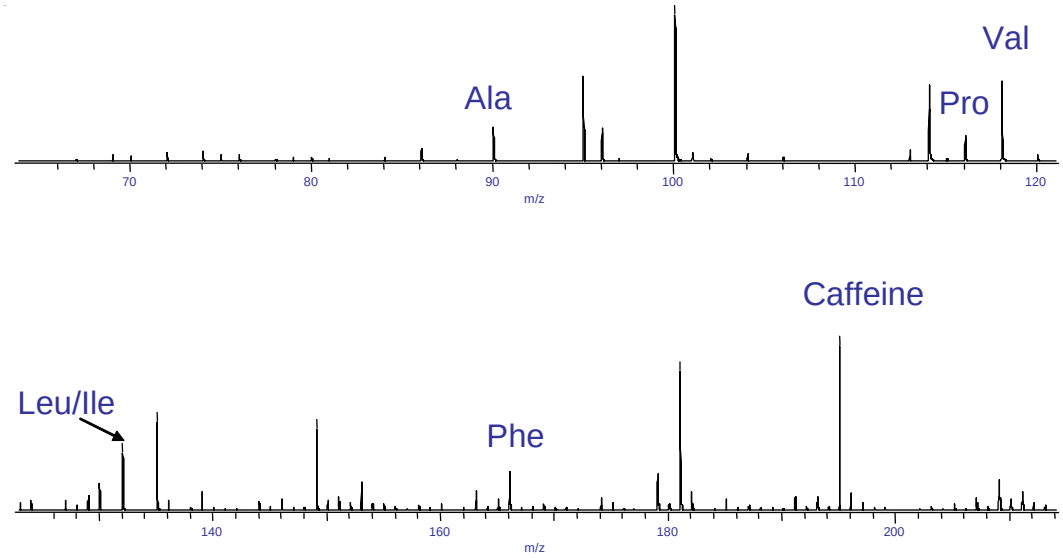

Figure 7. Amino acids and caffeine in saliva.

Analysis of other body fluids has been investigated briefly. Figure 7 shows the detection of amino acids and caffeine in a saliva sample from a coffee drinker.

Detection limits for many compounds with no sample preparation or preconcentration are in the high ppb to low ppm range.

Conclusion

DART can be used to analyze biological fluids. Only a few drops of fluid are required for the analysis.

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