SPECIFIC RADIOACTIVITY DETERMINATIONS OF IONIC ORGANIC COMPOUNDS OF HIGH SPECIFIC ACTIVITY BY FAST ATOM BOMBARDMENT AND FIELD DESORPTION MASS SPECTROMETRY

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ABSTRACT

Carbon-14 and tritium labelled ionic organic compounds such as quaternary ammonium salts, steroid sulphates, bile acid conjugates, and oligopeptides have been analyzed for their label distribution and for their specific radioactivity by fast atom bombardment and field desorption mass spectrometry. No significant differences between the quantitative results with both techniques are found. The minimal specific radioactivities detectable by this approach are about 20 MBq $mmol^{-1}$ or 10 GBq $mmol^{-1}$ for compounds labelled with one atom of carbon-14 or one atom of tritium per molecule, respectively. Specific radioactivity determinations of highly labelled biochemicals are characterized by a precision and an accuracy in the region between 1 % and 5 %.

Key Words: specific radioactivity, mass spectrometry, field desorption, fast atom bombardment

INTRODUCTION

Direct isotope determination of radiolabelled organic compounds by mass spectrometry (MS) enables the measurement of their specific radioactivity. Using field desorption (FD) MS (1), this has been demonstrated for steroids (2), carbohydrates (3), amino acids (4), as well as for lipids (5) labelled with ^{14}C or ^{3}H. Specific activity determinations performed by this method are characterized by the following aspects:

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(i) The time consumption is reduced compared to methods combining the data derived from chromatography and liquid scintillation counting;

(ii) the distribution of the radiolabelled species is obtained in addition to specific radioactivity data;

(iii) the precision of the data is high, the coefficient of variation generally varies between 0.5 % and 3 % as typically found in isotope dilution experiments;

(iv) the accuracy of the data is good and in the same order as the precision, because isotope effects encountered in the mass spectrometric process generally are smaller than the typical precision achieved. Another beneficial aspect with respect to accuracy appears to be the principle that both labelled and nonlabelled species are measured through a common property, their mass, with one method in a single analytical run;

(v) the isotope analysis of fragment ions also can provide information about the position of the label, however, because of the possible scrambling of the label in case of ^{3}H, ^{3}H NMR is a better technique. This structural aspect was not investigated in the present study.

This study evaluates the applicability of fast atom bombardment (FAB) mass spectrometry (6) for quantitative measurements directed towards specific radioactivity determinations of biochemicals and compares results obtained by the application of both FAB and FD MS to the same samples.

RESULTS AND DISCUSSION

Organic Cations

Organic cations such as quaternary ammonium or sulphonium ions are directly amenable to mass spectrometric analysis using field desorption (7) even in case relatively crude extracts of biological origin are investigated (8). The sensitivity of FD MS in the positive ion mode for these types of cations is higher than for neutral organic compounds, obviously because preformed ions are investigated and no ionization or cationization process is necessary in this case. FAB MS in the positive ion mode also provides direct access and a high sensitivity for organic cations. Figure 1 presents the FD molecular ion region of a radiolabelled drug with a quaternary ammonium structure and Table 1 gives the calculated as well as the observed abundance data both for the nonlabelled and for the labelled compound as determined by FAB and FD MS in the positive ion mode.

The agreement between the calculated and the experimental FAB and FD pattern of the nonlabelled compound is good. In the measurements performed as basis for the data given in Table 1, the FAB spectra consistently showed the first isotope peak with a relative abundance of about 2 % below the calculated value, whereas the FD spectra virtually reproduced the calculated value. At the moment, this effect remains unexplained.

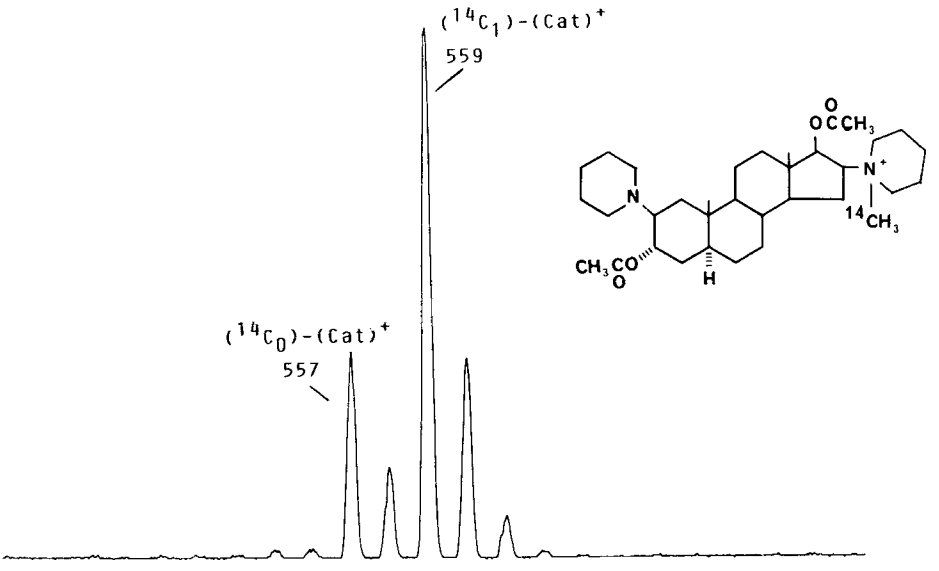

Figure 1: FD spectrum of Org NC 45 showing the region of the intact cation; sample amount ca. 200 ng.

Table 1: Isotopic abundances of the cation Org NC 45 determined by FD and FAB MS in the carbon-14 labelled and in the nonlabelled form compared to the calculated isotopic abundances.

m/z	calc.	nonlabelled FAB MS	nonlabelled FD MS	labelled FAB MS	labelled FD MS
555	-	7.4	2.8	3.0	1.2
556	-	3.4	2.0	2.3	1.2
557	100	100	100	41.1	38.6
558	39.80	37.8	39.8	18.1	16.9
559	8.52	7.8	8.5	100.0	100.0
560	1.29	1.1	1.3	36.2	37.5
561	0.15	-	0.4	9.8	7.9
562	-	-		2.2	1.4
	relative abundance [$^{14}C_0$]			26.0 %	26.9 %
	relative abundance [$^{14}C_1$]			74.0 %	73.1 %
	resulting specific activity			1.709	1.688 MBq mmol^{-1}

Surface reactions leading to $(M-2H)^+$ ions are more pronounced in the case of FAB than for FD MS, and this appears to be a general phenomenon (e.g. 9,10) For the calculation of the true relative abundances of the labelled and of the nonlabelled species a correction for the satellite peaks occurring on the low and on the high mass side has to be performed: (i) the amount of the low mass side correction should be derived directly from the mass spectrum of the labelled compound using the relative abundance of the satellite ion two mass units below the signal of the nonlabelled compound; (ii) the high mass side correction can be based on the calculated isotopic pattern, after having confirmed that this pattern is reproduced with the nonlabelled compound under identical experimental conditions. With these corrections a specific acitivity of 1.709 GBq $mmol^{-1}$ and of 1.688 GBq $mmol^{-1}$ is calculated using the FAB spectrum or the FD spectrum, respectively. Thus, both methods provide identical results as the difference of about 1 % is in the same order as the accuracy of the determination. These values are in good agreement with the specific acticity of the [^{14}C]methylbromide (1.8 GBq $mmol^{-1}$) used in the synthesis of the compound.

Organic Anions

The direct mass spectrometric analysis of strongly acidic compounds such as organic sulphate esters or sulphonates requires the application of field desorption (e.g. 11,12) or fast atom bombardment (e.g. 13) mass spectrometry. In the normal FD mode where positive ions are detected, these types of compounds show protonated ions or cluster ions generated by complexation with alkali ions, such as sodium or potassium. In contrast to FD, where the switchover to negative ion detection requires certain modifications (14), in the FAB source only inversion of the polarity of the applied potentials is required (15). Due to the relatively long stability of the FAB ion currents and due to the fast switchover of the instrument, often positive and negative ion FAB spectra can be obtained from the same sample loading. Figure 2 displays the result of such an analysis for [^{14}C]taurocholic acid.

The positive ion FAB spectrum of the radiolabelled taurocholic acid given in Figure 2a shows a variety of ion clusters in the mass region corresponding to the intact compound, of which the signals for the $(M+H)^+$, the $(M+Na)^+$, and the $(M+K)^+$ ion are the most prominent ones. These main groups are characterized by similar isotopic patterns, and they are accompanied by a number of unidentified satellite peaks, such as the signals at m/z 522, m/z 535, and those centered around m/z 572. Due to the isotopic distribution the latter either may represent a labelled impurity or a methodological artifact that is not simply explained by clustering with sodium

or potassium. The signals observed at m/z 553 and m/z 575 probably represent a glycerol matrix cluster plus its corresponding sodium complex. In contrast, the molecular ion region of the negative ion spectrum in Figure 2b shows the $(M-H)^-$ ion as the only intense signal, probably because strongly acidic compounds are present as anions in the glycerol matrix, a situation which can be regarded as an effective preionization (16,17) of the sulphate.

As shown in Figure 2, the quantitative evaluations of the $(M+H)^+$ and $(M-H)^-$ pattern result in specific activities of 1.81 GBq $mmol^{-1}$ and 1.80 GBq $mmol^{-1}$, respectively. Because of the simplicity of the negative ion spectrum and because of the virtually identical result using the protonated and the deprotonated molecular pattern this appears to be a highly reliable quantitative result, even in spite of the lower specific activity of 1.49 GBq $mmol^{-1}$ determined by the supplier using established methods, such as chromatography combined with radioactivity counting.

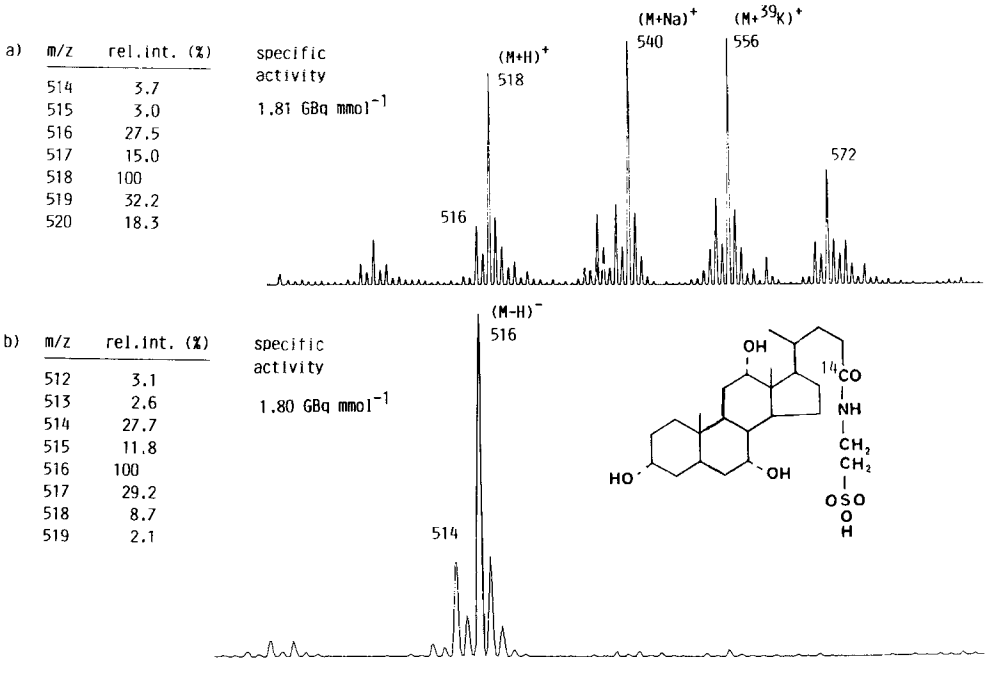

Figure 2: Partial FAB spectra of [24-^{14}C]-taurocholic acid; sample amount ca. 1 µg; matrix glycerol;
a) positive ion spectrum and quantitative evaluation of the $(M+H)^+$ ion group.
b) negative ion spectrum and quantitative evaluation of the $(M-H)^-$ ion group.

Due to the presence of overlapping signals of different origin on the m/z values of the nonlabelled species, a quantitative evaluation of the $(M+Na)^+$ and of the $(M+K)^+$ patterns results in a false low value for the specific activity.

With regard to the analysis of sulphate esters, which form an important class of conjugates in the urinary excretion of exogenous and endogenous compounds, the introduction of FAB MS has facilitated the direct mass spectrometric detection of these compounds considerably. Whereas ion production from sulphate ester samples in FD MS is strongly hampered by the presence of equimolar or higher amounts of alkali cations (12), fast atom bombardment appears to tolerate alkali salt contaminations much better. In the negative ion mode, intense signals for the corresponding $(M-H)^-$ ions are readily detected in the FAB mass spectra of sulphate esters. As an example, Figure 3 gives the molecular ion region of [7-^{3}H] dehydroepiandrosterone sulphate.

There is accidental overlap between the nominal masses of the $(M-H)^-$ ion of nonlabelled dehydroepiandrosterone sulphate and that of the glycerol matrix cluster $(glycerol_4+H)^+$ at m/z 367. Glycerol matrix cluster ions

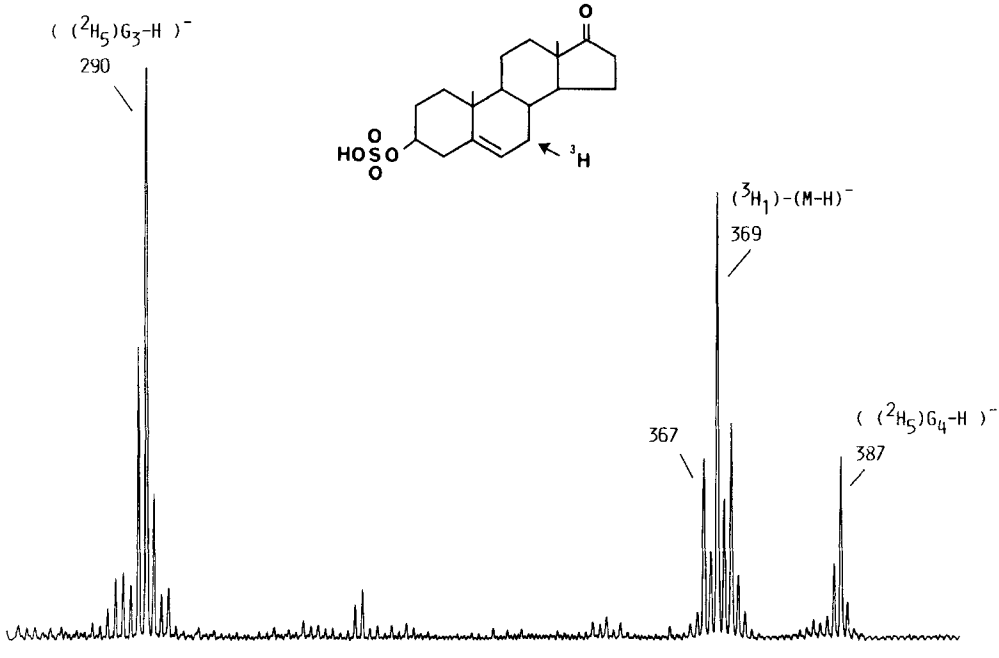

Figure 3: Partial negative ion FAB spectrum of [7-^{3}H]dehydroepiandrosterone sulphate; sample amount ca. 80 ng; matrix [$^2H_5$]glycerol.

can be completely suppressed by establishing an analyte monolayer on the matrix surface (18); however, using sample amounts in the order of 100 ng or smaller, as available for the analysis given in Figure 3, these conditions are not reached. Thus, to circumvent an overlap between analyte and matrix ions, pentadeuterated glycerol was used as matrix. With this compound, the matrix clusters containing three and four glycerol molecules are found at m/z 290 and m/z 387, respectively, as shown in Figure 3. Under these experimental conditions the $(M-H)^-$ for dehydroepiandrosterone sulfate is found in a mass region virtually free of matrix ions, and the three ion signals at m/z 367, 369, and 371 specifically represent the molecular species of dehydroepiandrosterone sulphate containing no, one, or two tritium atoms. Evaluation of the pattern given in Figure 3 gives a specific activity of 1.129 TBq $mmol^{-1}$ being about 13 % below the specified value of 1.295 TBq $mmol^{-1}$ determined by the manufacturer of the compound.

Zwitterionic Compounds

Oligopeptide analysis was the first area to which fast atom bombardment has been applied advantageously on a broad scale. Molecular weight and structural information (18-20) can systematically be derived from the positive and negative ion FAB spectra. In many cases, the isotopic patterns of the molecular species in these spectra appeared to be in agreement with those expected for the protonated or metal-cationated species. As an example for a good agreement between FAB experimental abundance data and those calculated using the natural isotopic abundances is given in Figure 4 for the synthetic hexapeptide Org 2766. Figure 4 is confined to the positive ion mode, as the negative ion spectrum provides a significantly lower sensitivity.

However, there is evidence (21,22) that the sputtering process in FAB also may induce some additional reactions beside the prevailing processes of cluster ion formation with protons, alkali metals, and protonated matrix or sample molecules. One of these reactions appears to be a combined proton/hydrogen or metal cation/hydrogen transfer resulting in relative abundances of the first isotope peak in excess of the calculated value. With regard to oligopeptide analysis, this effect appears to be favoured for contaminated samples and in analyses using low sample/matrix ratios, i.e. low amounts of sample. In quantitative evaluations of FAB spectra showing this effect a correction can be performed as demonstrated in Table 2, giving the evaluation of the $(M+H)^+$ ion group of the hexapeptide Org 2766 in a tritium labelled form.

H-L-Met(O_2)-L-Glu-L-His-L-Phe-D-Lys-L-Phe-OH

m/z	rel.int. (%) calculated	rel.int. (%) observed
868	-	5.6
869	-	7.4
870	100	100
871	50.1	49.8
872	19.0	20.1
873	5.3	6.7

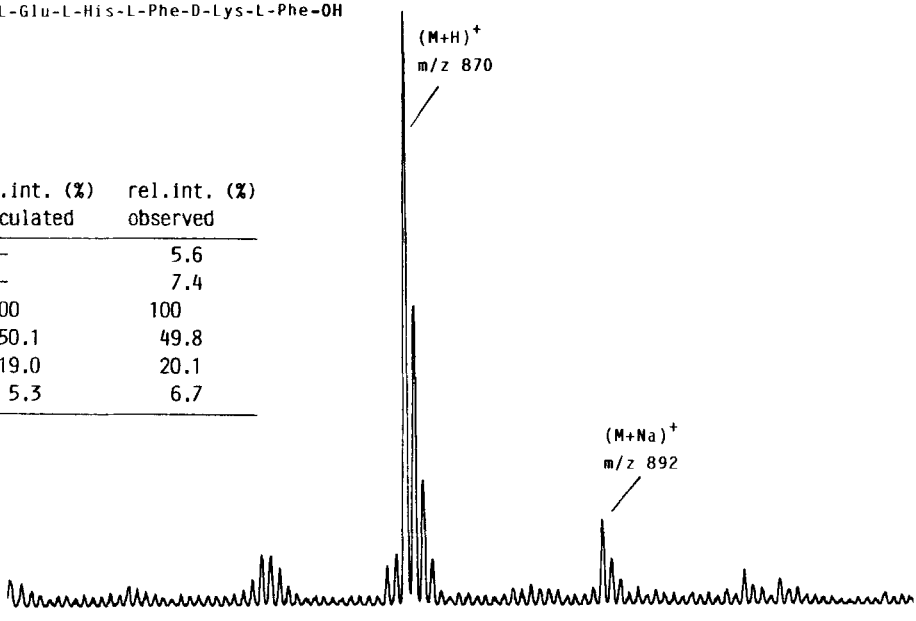

Figure 4: Partial positive ion FAB spectrum of the nonlabelled hexapeptide Org 2766; sample amount ca. 200 ng; matrix thioglycerol.

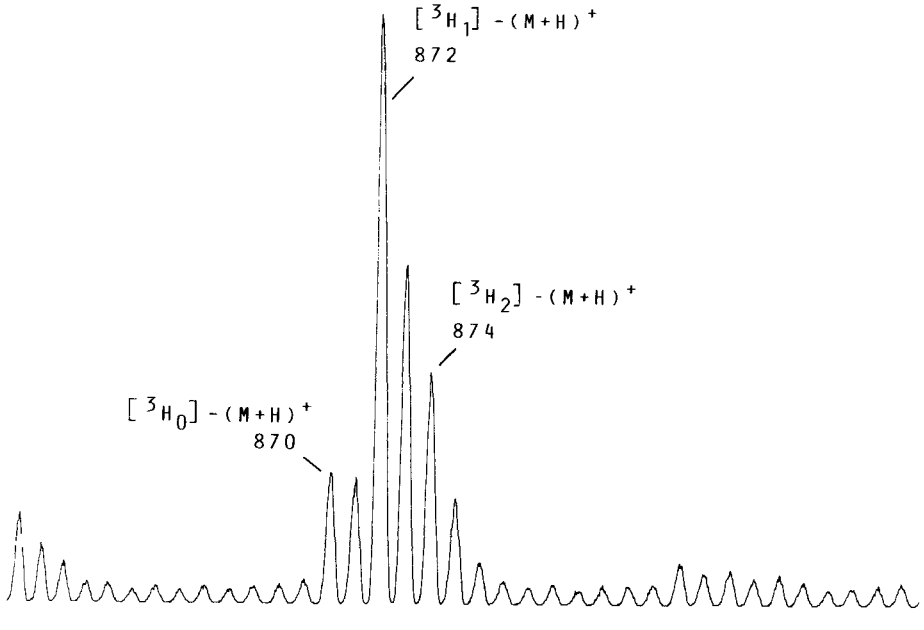

Figure 5: Protonated molecular group of the tritiated hexapeptide Org 2766 produced by FAB MS; sample amount ca. 400 ng; matrix thioglycerol.

NMR analyses, both ^{1}H and ^{3}H, indicated that the peptide contained about 1.0 ^{3}H/molecule in the phenylalanine residue and about 0.1 ^{3}H/molecule in the histidine residue. Figure 5 shows that the main constituent of tritiated Org 2766 is indeed a $[^{3}H_1]$-labelled species accompanied by smaller amounts of nonlabelled and doubly-labelled material. Careful inspection of the ion pattern in Figure 5 gave an elevated abundance for the (M+H+1) signal by about 7 % and this corrected pattern given in Table 2a is used as basis for the evaluation of the pattern in Figure 5. The good fit between the reconstructed and the experimental pattern evident from Table 2b supports this approach, resulting in a specific activity 1.067 TBq $mmol^{-1}$. A value of 0.932 TBq $mmol^{-1}$ was determined by high pressure liquid chromatography and counting with a precision of +- 20%, mainly due to

Table 2: Calculation of specific radioactivity of the tritiated oligopeptide Org 2766 using the FAB spectrum given in Figure 5:

a)Experimental isotopic pattern used as basis for the quantitative evaluation
b)Quantitative evaluation of the ion pattern given in Figure 3 with respect to the relative contribution of the nonlabelled, the singly, and doubly tritiated species of Org 2766 and comparison of the reconstructed and the experimental ion abundance pattern. (rel.int.: relative intensity; expt.: experimental; recon.: reconstructed; diff.: difference)
c)Calculation of the specific activity of Org 2766.

a)

species	(M+H-2)	(M+H-1)	(M+H)	(M+H+1)	(M+H+2)	(M+H+3)
rel.int (%)	5.6	7.4	100	57.5	23.3	6.4

b)

m/z	rel.int. expt.(%)	$[^{3}H_0]$	$[^{3}H_1]$	$[^{3}H_2]$	recon. pattern	diff.(%) recon.- expt.
868	2.1	0.9	-	-	0.9	- 1.1
869	2.9	1.2	-	-	1.2	- 1.7
870	20.9	15.6	5.4	-	21.0	+ 0.1
871	20.1	9.0	7.1	-	16.1	- 4.0
872	100	3.6	95.5	0.9	100	0
873	56.8	1.0	54.9	1.3	57.2	+ 0.4
874	38.9	-	22.3	16.5	38.8	- 0.1
875	16.6	-	6.2	9.5	15.7	- 0.9
876	5.0	-	1.1	3.8	4.9	- 0.1

c)

species	rel.abundance(%)	rel.specific activity
$[^{3}H_0]$	12.3	0
$[^{3}H_1]$	75.1	799.1
$[^{3}H_2]$	12.6	268.2
		specific activity 1,067.3 TBq $mmol^{-1}$

absorption effects of the peptide during chromatography. Combined use of ^{1}H and ^{3}H nuclear magnetic resonance revealed a specific activity of 1.11 TBq $mmol^{-1}$ with a precision of about +- 10 %. Thus, these data are in good agreement within the error limits of the experimental methods employed.

Intact oligopeptides also can be analyzed by FD MS, however, for the two radiolabelled samples presented in this section FD MS gave no useful results.

A characteristic feature of FAB mass spectrometry is its ability to ionize high molecular weight compounds demonstrated, for instance, by molecular weight determinations approaching 10,000 mass units (23). Unit mass resolution of molecular ion groups, which is required for label determinations, has been reported for molecular weights up to several thousand mass units. As an example for a direct isotope determination of FAB in the mass region above 1,000 mass units, Figure 6 shows the analysis of a tritium labelled dodecapeptide in the FAB positive ion mode, which was selected as it provided spectra of higher absolute intensity than the negative ion mode.

A comparison of the spectra of labelled Org 5878 in Figure 6b with that of the nonlabelled analogue directly shows the simultaneous presence of nonlabelled, singly, doubly, and triply labelled material. By theory, labelled

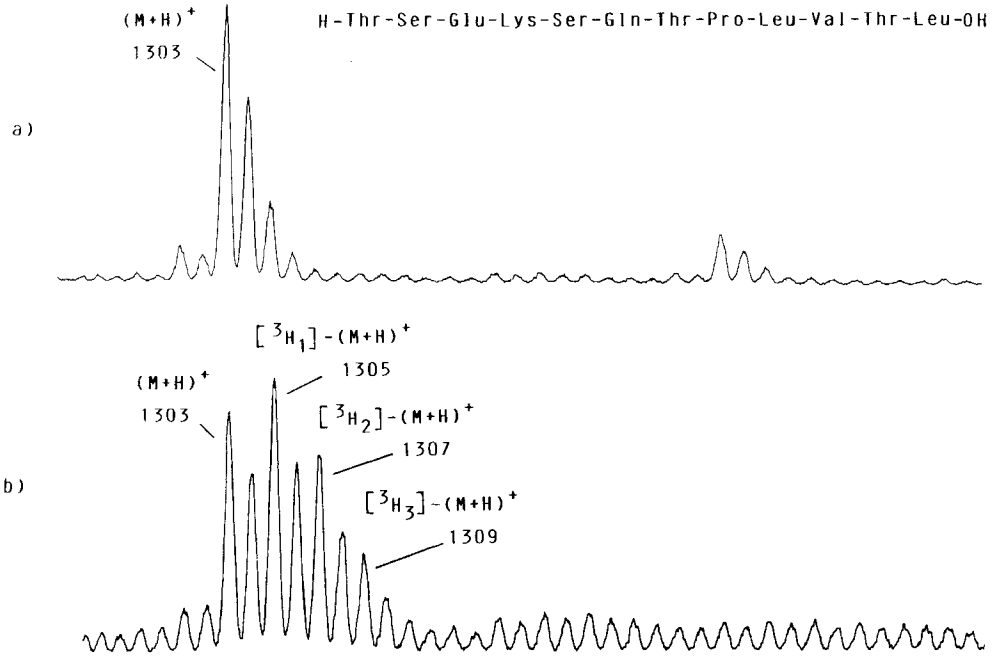

Figure 6: Partial FAB positive ion mass spectra of the dodecapeptide Org 5878; sample amount ca. 300 ng; matrix glycerol/thioglycerol ca. 1:1; a) nonlabelled Org 5878; b) tritium-labelled Org 5878.

Table 3: Abundance and specific radioactivity data derived from 3 different FAB positive ions spectra of the tritium-labelled dodecapeptide Org 5878.

species	spectrum 1		spectrum 2		spectrum 3	
	rel.ab. (%)	rel.spec.ac. (GBq $mmol^{-1}$)	rel.ab. (%)	rel.spec.ac. (GBq $mmol^{-1}$)	rel.ab. (%)	rel.spec.ac. (GBq $mmol^{-1}$)
$[^3H_0]$	31.1	0	35.7	0	32.8	0
$[^3H_1]$	36.5	388.5	33.2	353.4	37.2	395.9
$[^3H_2]$	23.4	498.0	21.9	466.2	21.0	447.0
$[^3H_3]$	9.1	290.5	9.2	293.8	9.1	290.5
specific activity (GBq $mmol^{-1}$)	1,177.0		1,113.4		1,133.4	
average specific activity (n=3)			1,141.3 +- 32.5 GBq $mmol^{-1}$			

Org 5878 also could contain 4 tritium atoms, however, the FAB mass spectrum does not indicate the presence of such a labelled species. The isotopic pattern of the nonlabelled compound was found to be in good agreement with the calculated one and no alteration of this typical pattern could be found in the FAB spectrum of the labelled compound. This spectrum, however, showed a significantly enhanced level of the so-called chemical noise background ions probably due to a reduced purity compared to the nonlabelled compound. To compensate for this effect, the baseline for ion abundance measurements in this spectrum arbitrarily was set at 50 % of the average intensity of these background signals. With this approach, three FAB spectra accumulated subsequently using a single sample loading were evaluated for the relative abundances of the differently labelled species using the calculated isotopic pattern and the high mass and low mass correction as described above. The results are given in Table 3. Although there is some variation in the relative abundance of the individual molecular species, the resulting data for the specific activity show a relatively small variation: The relative difference of the highest and the lowest value differ by about 5.5 %, and the approximated standard deviation of the average of 1.141 TBq $mmol^{-1}$ is about 2.8 %.

EXPERIMENTAL

Chemicals

Glycerol 99.5+%: EGA-Chemie, Steinheim, FRG. Monothioglycerol 98%: Sigma, St.Louis, Mo., USA.

Radiochemicals

The radioactivity data are given in Bq (37 MBq equivalent to 1 mCi).

[N-$^{14}CH_3$]-Org NC 45 (1-[(2β,3α,5α,16β,17β)-3,17-bis(acetyloxy)-2-(1-piperidinyl)-androstan-16-yl]-1-methylpiperidinium bromide) was prepared by reaction of [^{14}C]bromomethane (1.8 GBq mmol^{-1}) with (2β,3α,5α,16β,17β)-2,16-di-1-piperidinyl-androstane-3,17-dioldiacetate. Concentration 1.1 MBq ml^{-1} dichloromethane, corresponding to 650 nmol ml^{-1}.

[24-^{14}C]-Taurocholic acid: New England Nuclear, Boston, Mass., USA, product no. NEC-665, lot no. 1336-114, specific activity 1.49 GBq mmol^{-1}, concentration: 0.74 MBq ml^{-1} methanol/ethanol (1:3, v/v) corresponding to 500 nmol ml^{-1}.

[7-^{3}H]-Dehydroepiandrosterone sulphate, ammonium salt: New England Nuclear, Boston, Mass., USA, product no. NET-121, lot no. 1461-214, specific activity 1,295 TBq mmol^{-1} concentration: 37 MBq ml^{-1} ethanol, corresponding to 29 nmol ml^{-1}.

[^{3}H]-Org 2766 (H-Met(O_2)-Glu-His-Phe-D-Lys-Phe-OH) was prepared by reaction of $^{3}H_2$ with (Phe(I))^4-Org 2766 in the presence of Pd/C plus Pd/$CaCO_3$ (23). According to ^{3}H NMR the position of the ^{3}H was 91 % at C(4) of the phenylalanine residue and 9 % at C-(2) of the imidazole ring of the histidine. The concentration was 37 MBq ml^{-1} water/methanol (97.5:2.5 v/v) corresponding to 40 nmol ml^{-1}.

[^{3}H]-Org 5878 (β-endorphin (6-17), H-Thr-Ser-Glu-Lys-Ser-Gln-Thr-Pro-Leu-Val-Thr-Leu-OH) was prepared by reaction of $^{3}H_2$ with (2,6-diamino-hexynoic acid)-β-endorphin 6-17 in the presence of Pd/C (24). The position of ^{3}H was according to ^{3}H NMR exclusively at the β- and γ-positions of the lysine residue. The concentration was 37 MBq ml^{-1} water/2-mercaptoethanol (95.5:0.5 v/v) corresponding to 32.5 nmol ml^{-1}.

Mass Spectrometry

Mass spectrometric measurements were performed on a double focussing instrument type VG ZAB-1F (VG Analytical, Altrincham, England) in the double focussing mode. The instrument was equipped with a FD/FAB pushrod introduction system and a saddle field ion gun plus power supply (Ion Tech Ltd., Middlesex, England) modified by VG for neutral atom beam production. The atom gun was mounted on a laser port of the ion source housing. Xenon (Linde minican, Linde AG Unterschleissheim, FRG) was used as collision gas. The FAB targets used were plain stainless steel plates with dimensions of 5x1.4 mm supplied by VG Analytical. These were mounted to obtain an angle of incidence for the atom beam between 45^{0} and 60^{0}.

The samples were applied to the FAB target as solutions with the concentrations given above under optical control with a stereomicroscope at a

magnification of 40x using a 10 μl syringe. To prevent sample losses a rectangularly shaped teflon coated needle shaft was used for the sample application procedures. After transfer to the FAB target the solvents were evaporated to dryness either spontaneously or under a gentle stream of air at ambient temperature. Subsequently 0.2 - 0.5 μl of glycerol or thioglycerol was transferred to the FAB target.

Compared to the investigation of volatile radiolabelled compounds the problem of mass spectrometer contamination is strongly reduced in case nonvolatile compounds are investigated as performed in the present study: in fast atom bombardment MS the vast majority of the sample is still present on the target at the end of the measurement. Under FD conditions the contamination can be limited by restricting the emitter heating current to the range required for ion production and by avoiding the commonly employed pyrolytic cleaning of the FD wire after the investigation of a radiolabelled compound.

The mass spectra were accumulated using a multichannel analyzer type Canberra series 80 combined with a Canberra digitizer type 6271. For recording of the mass spectra between 10 and 50 repetitive magnetic scans were accumulated. Quantitative evaluation of the mass spectra was performed on a microcomputer type CBM 8032 interfaced with the Canberra multichannel analyzer.

CONCLUSION

Table 4 summarizes the results determined in this study by specialized mass spectrometric methods and gives a comparison of these data with those determined by more conventional techniques showing that in general a satisfactory agreement is observed.

Specific radioactivity determinations of carbon-14 or tritium labelled compounds by fast atom bombardment or field desorption mass spectrometry appear to provide improvements over established procedures with respect to precision, accuracy, and time consumption. The use of mass spectrometry minimizes a possible interference resulting from labelled impurities and the frequently troublesome determination of small mass-amounts is not necessary. Among the drawbacks of the technique presented are the high costs for the instrumentation required and the fact that only relatively high specific activities can be determined. With respect to very low specific activities, the mass spectrometric methods presented are confined to values exceeding 20

Table 4: Summary of radioactivity data determined in this study by MS and corresponding data determined by a combination of chromatography and counting (C+C) or nuclear magnetic resonance (NMR).

compound	specific activity by MS	specific activity by other methods
[^{14}C] Org NC 45	1.709 GBq mmol^{-1} 1.688 GBq mmol^{-1}	1.8 GBq mmol^{-1} for active starting material
[^{14}C] taurocholic acid	1.81 GBq mmol^{-1} 1.80 GBq mmol^{-1}	1.49 GBq mmol^{-1} (C+C)
[^{3}H] dehydroepiandrosterone sulfate	1.129 TBq mmol^{-1}	1.295 TBq mmol^{-1} (C+C)
[^{3}H] Org 2766	1.067 TBq mmol^{-1}	0.93 TBq mmol^{-1} (C+C) 1.11 TBq mmol^{-1} (NMR)
[^{3}H] Org 5878	1.141 TBq mmol^{-1}	not determined

MBq mmol^{-1} for carbon-14 activities and 11 GBq mmol^{-1} for tritium activites. High specific activities can be determined with a precision and accuracy of 1 % - 5 %, depending upon parameters such as sample amount, purity, and molecular weight. With respect to specific radioactivity determinations of biochemicals up to molecular weights of several thousand mass units, fast atom bombardment opens up a broad variety of applications.

REFERENCES

1. Schulten H.R. - Int. J. Mass Spectrom. Ion Phys. 32: 97 (1979)
2. Schulten H.R., Müller R., O Brien R.E., and Tzodikov N. - Fresenius Z. Anal. Chem. 302: 387 (1980).
3. Altman L.J., O'Brien R.E., Gupta S.K., and Schulten H.R. - Carbohydr. Res. 87: 189 (1980)
4. Schulten H.R. and Lehmann W.D. - Biomed. Mass Spectrom. 7: 468 (1980)
5. Lehmann W.D. and Kessler M. - Fresenius Z. Anal. Chem. 312: 311 (1982)
6. Barber M., Bordoli R.S., Sedgwick R.D., and Tyler A.N. - J. Chem. Soc. Chem. Commun. 7: 325 (1981)
7. Brent D.A., Rouse D.J., Sammons M.C., Bursey M.M. - Tetrahedron. Lett. 4127 (1973)

8. Lehmann W.D., Schulten H.R., Schröder N. - Biomed. Mass Spectrom. 5: 591 (1978)
9. Lehmann W.D. and Kessler M. - Chem. Phys. Lipids 32: 123 (1983)
10. Przybylski M. - Fresenius Z. Anal. Chem. 315: 402 (1983).
11. Schulten H.R. and Lehmann W.D. - Anal. Chim. Acta 87: 103 (1976)
12. Lehmann W.D., Böttcher J., Bässmann H., Schüppel R., and Schiebel H.M. - Biomed. Mass Spectrom. 9: 477 (1982)
13. Liehr J.G., Beckner C.F., Ballatore A.M., and Caprioli R.M. - Steroids 39: 599 (1982)
14. Zwinselmann J.J., Fokkens R.H., Nibbering N.M.M., Ott K.H., and Röllgen F.W. - Biomed. Mass Spectrom. 8: 312 (1981)
15. Barber M., Bordoli R.S., Sedgwick R.D., and Tyler A.N. - Biomed. Mass Spectrom. 8: 492 (1981)
16. Barber M., Bordoli R.S., Elliott G.J., Sedgwick R.D., and Tyler A.N. - Anal. Chem. 54: 645A (1982)
17. Williams D.H., Bradley C.V., Bojesen G., Santikarn S., and Taylor L.C.E. - J. Amer. Chem. Soc. 103: 5700 (1981)
18. Barber M., Bordoli R.S., Sedgwick R.D., Tyler A.N., and Whalley E.T. - Biomed. Mass Spectrom. 8: 337 (1981)
19. Williams D.H., Bradley C.V., Santikarn S., and Bojesen G. - Biochem. J. 201: 105 (1982)
20. König W.A., Aydin M., Schulze U., Rapp U., Höhn M., Pesch R., and Kalikhevitch V.N. - Int. J. Mass Spectrom. Ion Phys. 46: 403 (1983)
21. Barber M. - 9th Intern. Mass Spectrom. Conf. Vienna, 30.Aug.-3.Sept.82, keynote/2.
22. Barber M., Bordoli R.S., Sedgwick R.D., Tyler A.N., Green B.N., and Parr V.C. - VG Analytical Publ. Insight 10 (1980)
23. Barber M., Bordoli R.S., Elliott G.J., Horoch N.J., and Green B.N. - Biochem. Biophys. Res. Commun. 110: 753 (1983)
24. Kaspersen F.M., van Rooy A.M., Wallaart J., and Funke C. - Recueil 102: 450 (1983)