Contents

Preface xv
About the Editor xvii

1 Introduction of Mass Spectrometry and Ambient Ionization Techniques 1
Yiyang Dong, Jiahui Liu, and Tianyang Guo
1.1 Evolution of Analytical Chemistry and Its Challenges in the Twenty-First Century 1
1.2 Historical Overview of Mass Spectrometry and Its Role in Contemporary Analytical Chemistry 5
1.3 Desorption/Ionization in Mass Spectrometry 12
1.3.1 Electronic Ionization (EI) 13
1.3.2 Chemical Ionization (CI) 14
1.3.3 Fast Atom/Ion Bombardment Ionization (FAB) 15
1.3.4 Electrospray Ionization (ESI) 16
1.3.5 Matrix Assisted Laser Desorption/Ionization (MALDI) 18
1.3.6 Field Desorption (FD) or Field Ionization (FI) 19
1.3.7 Plasma Desorption (PD) (ICP, LTP, DART) 19
1.4 Ambient Ionization and Direct Analysis in Real Time 21
1.4.1 Ambient Ionization 21
1.4.2 Direct Analysis in Real Time 24
1.4.2.1 Mechanisms 24
1.4.2.2 Parameters 27
1.4.2.3 Devices 29
References 30

2 DART Mass Spectrometry: Principle and Ionization Facilities 43
David Rondeau
2.1 Introduction 43
2.2 Metastable Gas Stream Formation 43
2.3 Ionization Mechanisms in Positive DART 45
2.3.1 Generation of Primary Ions by Ambient Air Ionization 46
2.3.2 Formation of the Protonated Molecules 50
2.3.3 Formation of the Ammonium Adducts 54
2.3.4 Formation of the Radical Cations and Their Fragments 55
2.3.5 Matrix Effects in DART Due to Sample Solvents 59
2.4 Ionization Mechanisms in Negative DART 65
2.4.1 Generation of Primary Ions by Ambient Air Ionization 65
2.4.2 Formation of Deprotonated Molecules 68
2.4.3 Formation of Radical Anions 69
2.4.4 Formation of Anionic Adducts 70
2.5 Some Parameters Affecting the DART Mass Spectra 71
2.5.1 Substitution of Helium by Nitrogen or Argon 71
2.5.2 The Temperature of the Gas Stream 75
2.5.3 The Internal Energy of Ions in DART-MS 76
2.6 Conclusion 78
References 78

3 Sampling and Analyte Enrichment Strategies for DART-MS 81
Wen Ma, Xianjiang Li, and Huwei Liu
3.1 Dilution Strategy for Sticky Sample Analysis 81
3.2 Purification Strategy for Eliminating the Matrix Interference 82
3.2.1 Liquid Phase Extraction 82
3.2.2 Solid Phase Extraction (SPE) 86
3.2.3 Solid Phase Microextraction (SPME) 87
3.3 Derivatization Strategy to Decrease Polarity and Enhance Volatility 89
3.4 Conclusions 91
References 91

4 Optimization of DART and Mass Spectrometric Parameters 97
Guohua Wu and Wushuang Li
4.1 Introduction 97
4.2 Effect of Working Gas Type, Gas Flow Rate, and Its Temperature 98
4.2.1 Gas Type 98
4.2.2 Gas Flow Rate 99
4.2.3 The Working Gas Temperature of DART Ionization Source 100
4.3 Effects of Grid Electrode Voltage and Sampling Speed 102
4.3.1 Effect of Grid Electrode Voltage 102
4.3.2 Effect of Sampling Speed 103
4.4 Effect of the Sampling Mode 104
4.4.1 Sampling Methods 104
4.4.2 Position and Angle of the DART Ion Source 105
4.5 Effect of Ion Mode 106
4.6 Effect of Solvent Type and Reagents 108
4.7 Summary 109
References 109
## Contents

5 Interfacing DART to Extend Analytical Capabilities 115

5.1 Introduction 115

5.2 Interfacing DART with Different Separation Techniques 116

5.2.1 Solid Samples 116

5.2.2 Gaseous Samples 118

5.2.3 Liquid Samples 119

5.2.3.1 Liquid Chromatography 119

5.2.3.2 Capillary Electrophoresis 123

5.3 Techniques of Interfacing DART with Other Analytical Techniques 125

5.3.1 Surface Plasmon Resonance 125

5.3.2 Ion Mobility Spectrometry 126

5.4 Conclusion and Perspectives 129

References 129

6 Application of DART-MS in Foods and Agro-Products Analysis 133

6.1 Introduction 133

6.2 Applications of DART-MS in Agriculture and Food Science 134

6.2.1 DART-MS in Pesticide Residue Analysis 134

6.2.1.1 Fast Screening Purposes 134

6.2.1.2 Screening Highly Hazardous Pesticides in Agrochemical Formulations 140

6.2.1.3 Quantitative MRM Residue Method 147

6.2.2 Veterinary Drug Residue Detection 148

6.2.3 Fast Detection of Melamine in Milk 149

6.2.4 Detection of Mycotoxins in Cereals 150

6.2.5 Food Component Rapid Analysis 151

6.2.6 Contaminations in Food Contact Materials (FCMs) 156

6.3 Conclusion 156

References 157

7 Application of DART-MS for Industrial Chemical Analysis 163

7.1 Application on Household Items 163

7.1.1 Polydimethylsiloxane (PDMS) Analysis in Articles for Daily Use 163

7.1.2 Identification of Sulfides in Drywall 165

7.1.3 Phosphoric Acid Esters Screening in Aqueous Samples 168

7.2 Application on Food Packaging Safety and Quality Control 172

7.2.1 Identification of PDMS in Food Packaging Materials 172

7.2.2 Identification of Polymer Additives in Food and Food Packaging Materials 175

7.2.3 Identification of Residue Primary Aromatic Amines (PAAs) in Food Packaging Materials 176

7.3 Application on Pharmaceutical Products 177

7.3.1 Toxic Glycols Identification 177
Contents

7.3.2 Identification of Active Ingredients in Chinese Herbal Medicines 179
7.4 Application on Cosmetics Quality Control 182
7.4.1 Screening of Glucocorticoids Illegal Addition 182
7.5 Application on Other Industrial Chemical Fields 184
7.5.1 Ink Discrimination on Questioned Document 184
7.5.2 Ionic Liquids Identification 189
7.6 Conclusions 190
References 190

8 Application of Direct Analysis in Real Time Coupled to Mass Spectrometry (DART-MS) for the Analysis of Environmental Contaminants 193
Maxime C. Bridoux and Sébastien Schramm

8.1 Introduction 193
8.2 Screening and Quantitative Analysis of Pesticides 194
8.3 Flame Retardants DART-MS Analysis 204
8.3.1 Organophosphorus Flame Retardants (OPFRs) 204
8.3.2 Brominated Flame Retardants (BFRs) 207
8.4 Use of DART-MS for the Analysis of Personal Care Products (PCPs) 210
8.4.1 Screening of Organic UV Filters in Water 210
8.4.2 Screening of Phthalic Acid Diesters 211
8.4.3 HPLC-DART-MS Analysis of Parabens 211
8.5 Use of DART-MS for the Analysis of Aerosols 212
8.5.1 Online DART for Aerosols Analysis 212
8.5.2 Offline DART Methods 213
8.5.3 Advantages and Limitations of DART-MS for Aerosols Characterization 213
8.6 Miscellaneous Environmental Application of DART-MS 214
8.7 Conclusions 215
References 216

9 Application of DART-MS in Clinical and Pharmacological Analysis 223
Yue Li

9.1 Introduction 223
9.2 Sample Preparation 224
9.3 Applications of DART-MS 225
9.3.1 Rapid Determination of Small Organic Compounds in Biological Samples 225
9.3.1.1 Analysis of a Bitter Herbal Medicine Gentiana scabra Root Extract 225
9.3.1.2 Simultaneous Determination of 3-Chlorotyrosine and 3-Nitrotyrosine in Human Plasma 226
9.3.1.3 Rapid Screening for Methamphetamine, 3,4-Methylenedioxyamphetamine, and Their Metabolites in Urine 227
9.3.2 Newborn Screening for Phenylketonuria 227
9.3.3 DART-MS Analysis of Skin Metabolome Changes in Ultraviolet B-Induced Mice 228
9.3.4 Application in Detection of Breast Cancer 231
9.3.5 Transmission Mode DART-MS for Fast Untargeted Metabolic Fingerprinting 232
9.3.6 Applications of Confined DART Ion Source for Online In vivo Analysis of Human Breath 233
9.3.6.1 Real-Time Analysis of Exhaled Breath 234
9.3.6.2 Real-Time Monitoring of Oral Anesthetic Drug 235
9.4 Challenges and Limitations 236
9.5 Recent Advancements 237
References 238

10 DART-MS Applications in Pharmaceuticals 241
Karina G. Putri, Qianwen Wu, and Young P. Jang
10.1 Pharmaceutical Analysis 241
10.2 Quality Assurance 243
10.3 Illegal Active Pharmaceutical Ingredients and Counterfeit Drugs 244
10.4 Drug Development 247
References 251

11 Application of DART-MS in Natural Phytochemical Research 255
Vikas Bajpai, Awantika Singh, Brijesh Kumar, and Kunnath P. Madhusudanan
11.1 Introduction 255
11.2 Direct Analysis in Real Time (DART) Mass Spectrometry 256
11.3 DART-MS Parameter Optimization for Phytochemical Analysis 256
11.4 Applications of DART-MS in Phytochemical Research 257
11.4.1 Qualitative Phytochemical Analysis 257
11.4.2 Cell Culture Analysis 261
11.4.3 Analysis of Volatiles 261
11.4.4 Species Identification 262
11.4.5 Metabolic Profiling and Multivariate Analysis 263
11.4.6 Quantitative Analysis 274
11.5 Hyphenated DART-MS Techniques for Phytochemical Analysis 276
11.5.1 GC and HPLC-DART-MS 276
11.5.2 TLC/HPTLC-DART-MS 276
11.5.3 Capillary Electrophoresis-DART MS 277
11.5.4 DART-IMS-MS 277
11.5.5 Other Coupling Techniques 277
11.6 Improving Sensitivity of DART-MS for Phytochemical Analysis 278
11.6.1 Solvents and Gases 278
11.6.2 Matrix Suppression 279
11.7 DART-MS as Process Analytical Technology 279
11.8 Future Perspective 280
References 280
## Contents

### 12 Miscellaneous Applications of DART-MS  291
*Yoshihito Okada*

12.1 Introduction  291  
12.2 Usefulness of Negative-Ion Mode  292  
12.3 Application to Archeology and Conservation  293  
12.4 Application by Using TLC  293  
12.5 Application to Low Volatility, Chemical Warfare, and Homeland Security  294  
12.6 Pheromone Profiles from Live Animals in Parallel with Behavior  295  
12.7 Application to Distinction of Plants with Similarity  296  
12.8 Application to Space  298  
12.9 Application to Bituminous Coals  298  
12.10 Application to Detection of Nicotine  298  
12.11 Other Potential Applications of DART-MS  299  
12.11.1 Instantaneous Screening for Counterfeit Drugs with No Sample Preparation [26-1]  299  
12.11.2 Direct Analysis of Drugs in Pills and Capsules with No Sample Preparation [26-2]  300  
12.11.3 Detection of Lycopene in Tomato Skin [26-3]  300  
12.11.4 Distribution of Capsaicin in Chili Peppers [26-4]  302  
12.11.5 Detection of Unstable Compound Released by Chopped Chives [26-5]  302  
12.11.6 Rapid Detection of Fungicide in Orange Peel [26-6]  304  
12.11.7 "Laundry Detective": Identification of a Stain [26-7]  304  
12.11.8 Detection of the Peroxide Explosives TATP and HMTD [26-8]  306  
12.11.9 Instantaneous Detection of Explosives on Clothing [26-9]  306  
12.11.10 Rapid Detection and Exact Mass Measurements of Trace Components in a Herbicide [26-10]  308  
12.11.11 Rapid Analysis of *p*-Phenylenediamine Antioxidants in Rubber [26-11]  308  

Acknowledgment  309  
References  309  

### 13 Inherent Limitations and Prospects of DART-MS  313
*Tim T. Häbe, Matthias Nitsch, and Gertrud E. Morlock*

13.1 Aspects of Inherent Limitations of DART-MS  313  
13.1.1 Gas Settings  314  
13.1.1.1 Type of Gas  314  
13.1.1.2 Gas Temperature  314  
13.1.1.3 Gas Flow Rate  317  
13.1.2 Voltage of Electrodes  317  
13.1.3 Sample Introduction and Positioning  318  
13.1.4 Detection System and Mass Range  318  
13.1.5 Matrix Effects and the Need for Chromatography  319  
13.1.6 Buffer and Salt Effects  321  
13.1.7 Sample Carrier and Solvent  322  
13.1.8 Humidity Effects  322
13.1.9 Use of Isotopically Labeled Standards 322
13.1.10 Dopant and Derivatization 323
13.2 DART versus Other Ambient Ion Sources 324
13.3 Prospects of DART-MS 326
13.3.1 Automation and Miniaturized DART-MS 326
13.3.2 Sample Preparation, Preconcentration, and Introduction 327
13.3.3 Ion Focusing and Flexible Ion Transportation 327
13.3.4 Quantitative Surface Scanning and Imaging by DART-MS 328
13.3.5 Hyphenation of Effect-Directed Analysis and DART-MS 331
13.3.6 Thermal Separations by Temperature Gradients 331
13.3.7 Aerosol, in situ and in stillo Chemical Reaction and Kinetic Monitoring 332
13.3.8 High Resolution and Data Analysis 332
13.4 Concluding Remarks 333
References 333

Index 345