

# **GUANIDINES**

**Historical, Biological, Biochemical,  
and Clinical Aspects of the Naturally  
Occurring Guanidino Compounds**

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Historical, Biological, Biochemical,  
and Clinical Aspects of the Naturally  
Occurring Guanidino Compounds

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## PREFACE

In 1978, we had the first research meeting of guanidino compound analysis in Okayama, Japan. The purpose of the meeting was to standardize the methods of analyzing guanidino compounds, because the analytic methods, even, for example, that of normal plasma, were quite different from laboratory to laboratory at that time. More than ten laboratories joined in this research project. Thereafter, the purpose of the annual meetings was extended to cover general biochemistry of guanidino compounds, and every meeting has served to promote our mutual growth and progress. The last meeting of the Japan Guanidino Compounds Research Association in 1982 brought together more than 80 members, and about 30 papers were presented there. This, the 6th annual meeting, brings the International Symposium on Guanidino Compounds here to Tokyo.

Recently, many scientists are engaged in the research of guanidino compounds, especially in the field of clinical biochemistry. I am sure that the observation of guanidinosuccinic acid in the urine of uremic patients by Dr. Cohen's research group in 1963 ignited the recent exploration of the role of guanidino compounds in renal diseases.

The study of guanidino compounds does, however, have a long history. The first knowledge of guanidine was obtained by Strecker in 1861 (*Annalen der Chemie und Pharmacie*, 118, 151-177, 1981). He decomposed guanine with potassium chlorate and hydrogenchloride, and after isolating parabanic acid, oxaluric acid and xanthine from the reaction mixture, he isolated the sulfonic acid salt of an unknown base which he called "guanidine". We can find many reports on guanidine synthesis published during the following years.

The natural occurrence of guanidine was first reported by Schulze in 1892, who isolated it from the germ of a kind of pea (*Ber. Dtsch. Chem. Ges.* 65, 658-661, 1982 ). Today, guanidino compounds are known to be ubiquitous substances in plants as well as animals. These guanidino compounds are classified and reviewed by Dr. Robin in this symposium, including new guanidino

compounds she found, such as audouine, hirudonine, phascoline, phascolosmine and many phosphagenes.

We are very happy that such well-known scientists in guanidino compound research as Dr. Ronin and Dr. Cohen attended the meeting here in Tokyo and presented special lectures about their specialities.

In addition to their lectures, this symposium covers the following four sections:

The first section concerns analytical methods for guanidino compounds. Recently, high performance liquid chromatography for the determination of guanidino compounds has been developed and is now utilized widely in many laboratories. An analyzing system of the newest kind, a new idea for a fluorogenic reagent, and a new enzymatic method for methylguanidine estimation are reported in this section.

In the second section the metabolism of guanidino compounds in normal and abnormal organs, and in metabolic diseases, are discussed. We have many problems to be solved concerning the metabolism of guanidino compounds, including such basic problems as the metabolism of arginine to guanidino compounds, and the biosynthetic and regulatory mechanisms of guanidinosuccinic acid, guanidinoacetic acid or methylguanidine, especially regarding renal and hepatic failure. Current papers on argininemia also are considered in this section.

The physiological, pharmacological and toxicological aspects of guanidino compounds are discussed in the third section.  $\gamma$ -Guanidinobutyric acid induces convulsions in rabbits as reported by Mori and his colleagues in 1966. Subsequently it was observed that many guanidino compounds such as taurocyamine, glycoamine, N-acetylarginine, methylguanidine,  $\alpha$ -guanidino-glutaric acid, homoarginine and  $\alpha$ -keto- $\delta$ -guanidinovaleric acid could induce seizure activity in experimental animals. Several papers about methylguanidine and taurocyamine, i.e. guanidinoethane sulfonate, are presented in the session. The relationship of taurine to taurocyamine is one of the most interesting themes to be discussed.

In the last section, the involvement of guanidino compounds in acute and chronic renal failure are discussed. This is an urgent theme because of the vast number of patients with renal failure. Presently, guanidinosuccinic acid, guanidinoacetic acid and methylguanidine are used as indicators of renal function in clinical laboratories. Implications of these guanidino compounds in the pathogenesis of acute and chronic renal failure, including uremia, are discussed. Some prophylactic and thera-

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peutic treatments of guanidino compound anomalies are also reported in this section.

Finally, we thank the Ministry of Health and Welfare of Japan, the Pharmaceutical Association in Tokyo and Osaka, and the many contributors for their encouragement and financial support of our symposium.

A. Mori

## DEDICATION

It's been over twenty years since I first began meddling in uremic plasma looking for a hypoglycemic factor and stumbled upon a guanidino compound. I've carried on a love affair with the guanidines ever since but never realized there was anyone else out there interested until two years ago when I met Akitane Mori. He introduced me to a great mob of people dabbling in guanidines. I felt like a poor orphan raised by strangers who suddenly discovers his true family.

The orphan metaphor is all too appropriate since the guanidines are classic examples of the "medical orphan", an etiology in desperate search of a disease. The ensuing pages represent an effort to document that search. This text results from the proceedings of the International Symposium on Guanidino Compounds held in Tokyo, Japan on September 5-7, 1983 and is a product of the hard work and imagination of Professor Mori and his Organizing Committee. I would, therefore, dedicate this volume to the Guanidine Family and to Professor Mori who fathered this strange brood.

B.D. Cohen

## ACKNOWLEDGEMENTS

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