

# The Contemporary Arab Contribution to World Culture



# The Contemporary Arab Contribution to World Culture:

*An Arab-Western Dialogue*

Edited by

Magdi Youssef

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Edited by Magdi Youssef

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Participants of the IAIS Congress at the UNESCO in Paris, March 2009



Logo of the IAIS designed by the late Saad El-Girgawi, an Arab calligrapher and artist.





# CHAPTER ONE

## INTRODUCTION

MAGDI YOUSSEF

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### **Introduction**

These are no mere “proceedings” of a congress bearing a certain title. This is rather an argument bearing on the idea of Unity of Knowledge in our times. Therefore, the disciplines represented in this volume are representative of all branches or specializations of the arts and sciences in our present day: in the natural sciences, they are represented by pharmacology and industrial engineering, in the social sciences through political economy, and in the arts via architecture, which encompasses all sorts of plastic arts. And last not least, there is the field of contemporary literary discourse.

Yet the main concern of this volume is to challenge the impression, if not the common prejudice, either subtle or open, that contemporary production in all disciplines is only the privilege of the modern West, whereas Non-Western societies are thought to have nothing, or almost nothing to add to Western achievements in almost every respect.

Even though these non-Western societies are discriminated against and are socially and economically marginalized in our present-day world, they still have quite a lot to add to world knowledge in all disciplines and specializations. This very fact reminds me of my teaching experience in Egypt during the late nineteen seventies and early eighties at Tanta University. Tanta University is located in the middle of the Nile Delta and it is widely regarded as a provincial university recruiting its students from the neighboring agricultural areas. It is lacking so many of the services and resources dedicated to the capital of the country. But I felt closer to my students in that ‘provincial’ university than to those of Cairo, the capital,

who are much more privileged and yet much less avidly attempting to learn and to do research, compared to their peers in Tanta.

I am not necessarily drawing parallels between the marginalization on a global level and that on a national one, especially outside the Western hemisphere. But I want to address an illusion which exists in the minds of so many people, especially among the so-called educated, that the existing Eurocentric or Western standards and research results constitute an 'ideal' to be followed by all the other socio-cultures when dealing with nature and society. Such an illusory assumption does not only constitute a truly questionable belief in the West with regard to non-Western societies, but it is also widespread among so many members of the intelligentsia in non-Western societies.

It is for this reason that I have chosen the approach of an Arab-Western dialogue as a means of questioning and challenging the well-established stereotype of a West that must exclusively define scientific and scholarly standards. And to this end I have invited expert scholars from both the Arab World and the West to a scholarly meeting of the International Association of Intercultural Studies (IAIS) that took place at the UNESCO headquarters in Paris, France, in 2009. The papers presented in Paris and the proceedings of this meeting encompass a variety of representative disciplines. With regard to each of the disciplines discussed, an Arab scholar presented the results of his original research (or – as in the case of architecture - of his reflections on the innovative practical achievements in his discipline) while a Western expert added his critical commentary.

For the moment, there exists only a single exception to this rule in this first edition of the 'proceedings'. The Western commentary on Professor Dowidar's most valuable contribution to the analysis of the great economic crisis triggered by American banks in 2007/08 is still lacking, as we have to do without the comments originally verbally offered by Prof. Christian Sigrist (Münster University) who was incapacitated by his illness and sorely passed away afterwards. We are now waiting for an appraisal promised by Professor Michael Kraetke of Lancaster University that will critically focus on the politico-economic analysis of the global crisis offered by Professor Mohamed Dowidar (Alexandria University). It will be included in the planned second edition of this book.

To be honest, I have always wished to realize this scholarly meeting which materializes in a 'collective' way a cherished dream of mine, a dream embraced since my early youth, which expressed the desire to be able to specialize in 'all' disciplines alike. Which is obviously impossible in our times, even though our great ancestors, like Avicenna and Al-Farabi, could almost manage to do so. Yet the sheer ramifications of

knowledge in each discipline in modern times make it often very hard today to follow a research paper in a subsection of a branch of science that is different from one's 'own' specialization, let alone in a completely different field. This demonstrates the huge challenge I am facing with this volume, determined as I am to have recourse to the collective research work of all those experts of different disciplines, in order to be able to realize my objective of the Unity of Knowledge.

This volume is a provocative and challenging one. And therefore, it solicits discussion throughout. It is certainly hoped that it will inspire other similarly marginalized civilizations and socio-cultures worldwide to follow suit and give us, in a similar vein, examples of their contributions to world culture in all disciplines. To contribute to world culture certainly does not mean to 'start from scratch' (or even, to attempt to do so). Often, it may mean that one tries to draw on concretely existing – and often, inherited – solutions peculiar to one's specific socio-culture that arise out of its way of dealing with nature, either physically, socially or artistically. This especially in the three continents, Asia, Africa, and South as well as Central America. And why not also in each of the distinctive socio-cultures that exist in the 'Western World' itself? In doing so, we may in fact be re-testing the globalized norms that mostly stem from the West. Science can gain by drawing on one's own inherited pre-modern societal practices. As could be shown in the case of pharmacology, in this volume, certain norms of the U.S. Food and Drugs Administration (FDA) have been revised, and underlying assumptions have been corrected by having recourse to the empirical evidence and thus 'lessons' inscribed in inherited food consumption habits of Libyans rooted in their own traditional societies, as the Egyptian scholar of pharmacology, Professor M. Raouf Hamid has found while teaching and doing research at Al-Fatih University in Libya some thirty-seven years back.

The same rationale can be discovered in the attempt of Professor Hamed El-Mously, of the Faculty of Engineering of Ein-Shams University, to rely on the local populace, local knowledge and local renewable material resources of the Egyptian countryside in the context of a project that intends to sustain local societies and buttress the self-reliant position of especially women in those areas focused on, instead of having recourse to the abstract Western models, mostly embraced and reproduced by the United Nations' 'experts' that try to tell us how to 'develop' so-called 'backward oriental' societies. (This does not deny the possible plausibility of making use of either Western or non-Western inventions, in other words, of relevant insights wherever they may hail from, as long as this

choice springs from the *real needs* of human beings in the objectively varying *receiving context*.)

A corresponding rationale can also be encountered in a noteworthy approach to the housing situation of Egyptian agricultural workers that has been theoretically and empirically pursued by Hassan Fathy (1900 – 1987) in order to meet both social and ecological requirements that most of the ‘modern’ Western architectural approaches and ‘housing models’ failed to consider. Western-trained architects attempting to tackle the problems went for purely abstract, market-oriented designs which would cost a hell of a lot more and yet alienated the inhabitants from their inherited socio-cultural legacies and from the possibility of living in a far more intimate, psycho-socially and environmentally adequate ambiance. Similar challenges led to the reception of Fathy’s approach in Asia, West Africa, Arizona and South America. This example motivated the architect Rasem Badran, who acquired his PhD at one of the ‘top’ technological Universities in Germany, the Technische Hochschule Darmstadt, to revolt against - or at least take his distance from - the imported market-oriented abstract models of design, and to opt instead for the rationale inscribed in his native Arab-Palestinian-Jordanian traditional ways and forms of building peoples’ dwellings.

Both Rasem Badran and Hassan Fathy obtained their degrees at European universities. The latter studied architecture during the early decades of the 20th century at the Polytechnique in Paris. Both made use of their encounter with modern Western architectural tools and devices in order to develop a critical distance, and to re-discover the rationale of their native means of constructing dwellings in their own region.

The same approach was realized in the politico-economic analysis of Mohamed Dowidar, veteran Professor of Political Economy at Alexandria University in Egypt, when he produced his original interpretation of the massive global crisis triggered by the U.S. banks. This crash has usually been interpreted by Western analysts as a ‘financial’ one. Yet Dowidar’s seminal study has delivered the proof that it is in the first place the manifestation of a multifaceted global systemic crisis of a mode of production that is beset with a contradiction between the social nature of production and the private, incentive-based form of appropriation - a contradiction that has been irrationally dominating the present mode of production worldwide since its very outset, with all its risks, breaks and interruptions.

The fact that a researcher hails from a different socio-culture that is not identifying itself with the globalized modern Western mode of production, even though it is forced to deal with it and with its overwhelming

economic and juridical laws that are dominating everything almost everywhere (mainly through the world market), helps to recognize and therefore reveal various insights into the phenomenal contradictions mentioned above. Professor Dowidar stems originally from the countryside of the Nile Delta in Egypt and as such he is familiar with the native agricultural 'mode of production' in this region since his early childhood. How could he, as a mature scholar, distance himself as a thinker from his original setting, let alone allow himself to be identified with the Western modes of thinking, even though he makes use of Western tools of research? Hailing from his objectively different background, he had to come out with results different from those of the majority of his Western colleagues.

In my case, being a native Egyptian amply exposed to Western thought while teaching and doing research for decades at West German universities, it is, I think, apparent that I have found an alternative approach to the dominating Western research orientations in my way of interpreting the relationship of the various national literatures to each other and foremost to world literature.<sup>1</sup> I have advocated another approach, opposed to that of the acculturation theories, or those of an 'abstract reader' proposed by the Constance school, let alone the Western philologically oriented approaches in which not a lesser man than Edward Said himself has been almost completely embedded, as he was raised even back home, since his early childhood days, in the Western school system before emigrating to the US.<sup>2</sup> My approach is characterized instead by springing from what I call the "receiving socio-cultural context" that would be adding different perceptions to whatever it is 'receiving' in terms of 'alien' scientific research results, or in the form of 'alien' literary and artistic phenomena. My dear colleague Dr. Pflitsch, of the Free University of Berlin, has erroneously taken me, in his commentary on my paper, for an adherent of the hermeneutic trend of the Constance School, without realizing the deep divide between my approach, which stems from a social-scientific understanding of literary production and reception

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<sup>1</sup> See for instance my relatively recent study: *Decolonizing World Literature*, in: D'haen, Theo et al (eds): *Major versus Minor? languages and Literatures in a Globalized World*, John Benjamins Publishing Company: Amsterdam/Philadelphia, 2015, pp. 125-140.

<sup>2</sup> See my critique of Said's philological approach in my study: *The Myth of European Literature*, Symposium Press: Rotterdam and Aachen, 1998, pp. 30-32, see also its Italian version: *Il mito della letteratura europea* (pp.67-105), in: *La letteratura europea vista dagli altri* (a cura di Sinopoli, Franca), Meltemi Editore: Roma, 2003, especially pp. 87-90.

processes,<sup>3</sup> and the abstract hermeneutic one of Jauss and Iser in Constance. But such an amalgamating projection can easily take place by reducing radically different approaches to those of the dominant Western ones. Even the eminent German researcher and philosopher Juergen Habermas took me for an adherent of Jauss's hermeneutic approach when we met in Cairo during his visit to Egypt in 1997. So why not Andreas Pflitsch?! I have also fallen prey to such a cultural projection mechanism when projecting my native Egyptian socio-culture onto the Western, specifically Parisian one, while visiting the French capital for the first time when I was only 19. And yet, the more I became acquainted with French societal legacies, the less I became a victim of such cultural projections.

Needless to say that accurate scientific studies would help us to reveal the fallacy of such cultural projections, and would enable us to replace them by object-oriented recognition of juxtaposed socio-cultures.

At long last, the 'philosophy' of this exercise is to be summed up in the following tenet: What matters is, to start from one's own socio-cultural context when receiving whatever 'alien' cultures propose in all disciplines, and to be ready to re-consider and re-test those foreign cultural achievements in a methodological way that is springing from the *objective* difference of the receiving socio-culture. The accurate awareness of the objective difference of one's own socio-culture from that of the received one(s) would considerably enhance the possibility of adding new perspectives to those inscribed in the received culture(s) while being all the more rooted in one's original socio-culture. This stance would all the same lead to an enrichment of world culture. Such an alternative approach based on the full recognition of the variety of socio-cultures would be most refreshing and thus likely to invigorate human creativity in all disciplines worldwide.

In other words, the main issue addressed here is that the present one-sided and one-dimensional orientation in almost all disciplines worldwide – from the natural sciences to the social sciences, and including most discourses on literature and the arts – is being mainly Western in origin. The West – *which West* ?- undoubtedly is the new Mekka of research and the source of prevalent world views in modern times, to which the new generations in the so-called Third World are predominantly taking refuge,

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<sup>3</sup> See my paper: From A Philological to A Social Scientific Approach with Regard to Comparative Literary Research, in: Coutinho, Eduardo F. (ed): Beyond Binarisms: Discontinuities and Displacements: Studies in Comparative Literature, selected papers from the 28<sup>th</sup> congress of the International Comparative Literature Association (ICLA), held in Rio de Janeiro from July 29 till August 4, 2007, Aeroplano: Rio de Janeiro, 2009, pp. 14-19 (large-sized pages).

while subjectively attempting to give up their original socio-cultural legacies and languages. This does not only eradicate the inherited variety of human ways of dealing with nature that stems from different requirements to meet the various objectively existing socio-cultural needs in their own right. But the West's easy-going indulgence in its hegemonial trends in the name of 'global interconnectivity' leads to an impoverishment of the historically evolved Western ways and means themselves.

This critique is neither a 'romantic' one that would remind us of Goethe's resistance to the emerging Newtonian vision of the World – a vision that is, according to Goethe's judgment, 'violating' the intimacy of the apperception of nature, as represented in his "Farbenlehre" (theory of colours) that he opposed by *coining* his concept of *Weltliteratur* –, nor is it denying Western achievements, including the Newtonian and Post-Newtonian ones.

My epistemological critique of the today's overwhelming orientation of World culture towards a *one-dimensional* Western culture is based on an alternative proposition that contrasts with the one that is reigning today: Do not start, in the first place, from the body of research produced and encompassed by given individual disciplines (with all their ramifications) that have set standards worldwide, but spring – as a researcher rooted in a specific socio-culture – from your concrete (i.e., objective) socio-cultural context, guided by the quest to meet the sheer needs of *the majority* of your own populations.

I am working on this issue of *relinking* the long lost relations of most of the modern disciplines to their specific socio-cultural contexts by applying this approach to modern Arab-Western interactions in a variety of disciplines, starting in this book with a focus on research in the natural sciences today, and including discourses pertaining to the arts and literary productions . At the same time, I hope that the other socio-cultures that are dominated and often marginalized by the cultural hegemony of the West worldwide – like the Indian, the Philippine and Korean, the Thai, the Persian, and why not also the Turkish, the Greek and the Irish, too ? – would follow suit in attempting to change the pattern of dependence (and obliviousness of cultural specificities) inscribed in present-day overwhelmingly one-sided West-centered research in all disciplines. I hope that this book of collective research demonstrates a rational alternative to this questionable trend. See more about my project in the following link: [https://en.wikipedia.org/wiki/Magdi\\_Youssef](https://en.wikipedia.org/wiki/Magdi_Youssef)

Last but not least, I would like to acknowledge the great commitment and support of Andreas Weiland in the process of producing this book

(and reading its proofs!) as a token of old friendship that I value very much and am really grateful for. I would like to further thank Dr Tamer Lokman, of Badr University in Egypt, as well as Mr. Mustafa Ibrahim of the Faculty of Education of Ein-Shams University in Cairo for their help in meticulously proofreading this book manuscript.



**PART ONE –**

**THE CONTEMPORARY ARAB CONTRIBUTION  
TO WORLD CULTURE IN THE CURRENT  
NATURAL SCIENCES**

## CHAPTER TWO

# LOCALITY AS A SOURCE OF ORIGINALITY: A MODEL FROM PHARMACOLOGY. THE POSITIVE INFLUENCE OF CAPSAICIN (A COMPONENT OF THE LIBYAN TRADITIONAL FOOD HARISA) ON GASTRIC ULCER AND ON TRANSPORT ACROSS BIOLOGICAL MEMBRANES

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The summer of 1981 had witnessed two simple scientific contributions to the pharmacology of capsaicin, that were actually (as have been proved later on) introducing to the scientific communities of pharmacy and pharmacology two new unique, beneficial findings that were not preceded.

The first finding was the property that capsaicin enhances drug absorption (*Influence of capsaicin on buccal absorption of sulfathiazole*, Raouf Hamed et al., oral communication, the Abstracts Book, 8<sup>th</sup> international congress of pharmacology, Tokyo, Japan, 1981).

The second finding was capsaicin's potential of protection against peptic ulcer. (Raouf Hamed et al., *A protective effect of capsaicin against experimental induction of gastric ulcer in rats*, 41<sup>st</sup> International Congress of Pharmaceutical Sciences, Vienna, Austria, FIP 81 Abstracts Book, p.126).

The importance of these two preliminary works is, probably, not confined to their historical dimensions, as the socio-cultural circumstances that formed the environment and context of these two works (together with

the other related works done by the same authors during the years 1979 – 1984) unveil some hidden issues, or issues that are still somewhat fertile regarding the point of departure of scientific research in many of the African, Asian and South American countries.

Accordingly, the present paper is going to present the following:

- List of the works done.
- How and where these works started.
- The main pharmacologic knowledge about capsaicin at the time just before starting these works.
- The contributions that these works have introduced to the knowledge that had been existing when they were presented for the first time.
- Pathway(s) of the later development of the relevant knowledge.
- Possible lessons.

## **I. List of the works done**

### **(A) Works presented in international congresses**

1. Influence of capsaicin on buccal absorption of sulfathiazole.

The 8<sup>th</sup> International Congress of Pharmacology, Tokyo, July, 1981 (Abstract included in the Abstracts Book).

2. A protective effect of capsaicin against experimental induction of gastric ulcers in rats.

The 41<sup>st</sup> International Congress of Pharmaceutical Sciences, (FIP), Vienna, September, 1981 (the abstract is included in the Abstracts Book).

3. Influence of capsaicin on drug absorption and transport across biological membranes.

The 43<sup>rd</sup> International Congress of Pharmaceutical Sciences, Montreux, September, 1983 (the abstract is included in the Abstracts Book).

### **(B) Publications in periodicals**

1. Influence of capsaicin on drug absorption and transport across biological membranes.

I-Effect on buccal absorption of sulfathiazole.

J. Drug Res. J. Drug Res. Egypt, 16, 67 (1985).

[Note: Done at the Faculty of Pharmacy, Al-Fateh University (FPFU), Tripoli, Libya, 1979/80, and presented at the 8<sup>th</sup> International Congress of Pharmacology, Tokyo, 1981].

2. Ibid.

ii-Effect on gastrointestinal absorption of sulfamethazine sodium in rats. *J. Drug Res. J. Drug Res. Egypt*, 16, 73 (1985).

[Note: Done at FPFU, Tripoli, Libya, 1979/80, and presented at the 43<sup>rd</sup> International Congress of Pharmaceutical Sciences, Montreux, 1983].

3. Ibid.

iii-Effect on buccal absorption of glucose.

*J. Drug Res. J. Drug Res. Egypt*, 16, 77 (1985).

[Note: Done at FPFU, Tripoli, Libya, 1979/80, and presented before the 43<sup>rd</sup> International Congress of Pharmaceutical Sciences, Montreux, 1983].

4. Ibid.

iv- Effect on transport of glucose across frog's skin. *J. Drug Res. J. Drug Res. Egypt*, 16, 81 (1985).

[Note: Done at FPFU, Tripoli, Libya, 1980/81, and presented before the 43<sup>rd</sup> International Congress of Pharmaceutical Sciences, Montreux, 1983].

5. Effect of capsaicin on gastrointestinal absorption of acetaminophen.

*J. Drug Res. J. Drug Res. Egypt*, 16, 1, (1985).

[Note: Done at the National Organization for Drug Control and Research (NODCAR), Egypt, 1984, and presented at the annual scientific conference of the Egyptian Society of Pharmacology and Therapeutics, Alexandria, 1985].

6. Interaction of capsaicin with mixed function oxidizes: an in-vitro study interaction of capsaicin.

*J. Drug Res. J. Drug Res. Egypt*, 15, 253 (1984).

[Note: Done at the Institute of Toxicology, ETH and University of Zurich, 1983/84].

7. Interaction of capsaicin with mixed function oxidizes: ex-vivo and in-vivo study.

*J. Drug Res. J. Drug Res. Egypt*, 16, 29 (1985).

[Note: Done at the Institute of Toxicology, ETH and University of Zurich, 1983/84].

8. Influence of capsaicin on enzyme induction by phenobarbital in rats.

*J. Drug Res. J. Drug Res. Egypt*, 16, 61 (1985).

[Done at FPFU, Tripoli, Libya, 1981/82, and presented before the European Workshop on Drug Metabolism, Liege, 1982].

9. Evaluation of capsaicin mutagenicity by the Salmonella/mammalian microsome testing system.

*J. Drug Res. J. Drug Res. Egypt*, 18, 153 (1989).

[Done at the Institute of Toxicology, ETH and University of Zurich, 1983/84, and presented before the 19th Conference of the Pharmaceutical Society of Egypt, 1986].

10. Cytotoxicity of capsaicin.

J. Drug Res. J. Drug Res. Egypt, 18, 161 (1989).

[Done at the institute of Toxicology, ETH and University of Zurich, 1983/84, and presented at the 19th Conference of the Pharmaceutical Society, Egypt, 1986].

11. Effects of capsaicin on osmotic fragility of red blood cells in rats.

J. Drug Res. J. Drug Res. Egypt, 18, 169 (1989).

[Done at the Institute of Toxicology, ETH and University of Zurich, 1983/84 and presented at the 19th Conference of the Pharmaceutical Society, Cairo, 1989].

12. Effect of capsaicin on bleeding time in rats.

J. Drug Res. J. Drug Res. Egypt, 15, 207 (1985).

[Done at the Institute of Toxicology, ETH and University of Zurich, 1983/84].

13. The effect of capsaicin on the locomotor activity of rats in the residential maze.

J. Drug Res. J. Drug Res. Egypt, 15, 191 (1984).

[Done at the Institute of Toxicology, ETH and University of Zurich, 1983/84].

## **II. How and where was the start?**

In October 1978, the author had joined the staff of the Faculty of Pharmacy at Al-Fatih University, Tripoli, Libya, as a Lecturer in Pharmacology. By that time, the faculty was just a new one, with the most senior students starting their third academic year of undergraduate studies.

The author, then 30 years old, had to teach the second-year students their first course of pharmacology. Being a beginner in teaching, he had to ask the advice of the senior staff (the elder professors). The careful application of their advice did not help in stimulating the students' enthusiasm in learning pharmacology. Surprisingly, taking attendance of the students was the traditional way that was commonly practiced to keep them attending the classes. The author did not accept that tradition.

He felt that the real challenge is to have the students attending the lectures for the sake of learning and not due to compulsory attendance.

Accordingly, the author decided to rely on himself in discovering appropriate means of motivating the learning process. Fortunately, the Faculty of Education of that university was not too far from the Faculty of

Pharmacy. After two weeks of intensive readings about education, the author found out how far the on-going educational process was mostly a big malformation. He acquired an understanding about the essential modern concepts (and methods) of education. The major concept that he got firmly convinced of and therefore applied in his teaching was that the university student is a partner in the learning process and not a follower. As a result, radical changes were gradually taking place in the learning process of pharmacology. The outcome was well beyond the attendance records that he totally eliminated. As a result, the students became strongly interested in pharmacology to the extent that they asked for ways of modifying their training during the summer vacation (July and August) and expressed the desire to switch from working in pharmacy shops to training in pharmacological research.

Therefore, the students, along with their lecturer, became a research team. This was the first step in the first pharmacologic research work that took place at the Faculty of Pharmacy in Libya. It led to the above-mentioned pharmacological research works on capsaicin.

**The question now is: *Why capsaicin?***

The lecturer had to take into consideration several factors while selecting the research point (or the research project) that was to be tackled by the junior research team. A major factor was, as already mentioned, his contention that the students are partners in the educational process, and that the research activity is a part of the educational process itself.

Accordingly, he had to choose a research point that would help to let the students feel its importance and that would lead all the same to new contributions to knowledge. This consideration led him to choose *capsaicin*, the pungent principle in hot peppers that are called “capsicum”, as the subject of research. The research thus dealt also with “harisa” that is made mainly of red peppers and that constitutes the common part or ingredient of the three meals prepared each day by most people in Libya.

Based on the biological properties of capsaicin and the available knowledge in literature at the time, two research objectives were formulated from the very outset. One of them was to test the possible effect of capsaicin on drug absorption, while the other was to explore the truth regarding the widespread “COMMON SENSE” that capsaicin, being a pungent principle, leads to the incidence of peptic ulcers.

That was the first step which led to further steps later that year.

### **III. The main pharmacologic knowledge about capsaicin at the time just before starting those research works (in the late 1970s)**

Perhaps the most peculiar property of capsaicin that had been discovered before the 1980s was its ability to produce a desensitization of the nerve endings, following high or repetitive dosages (Jancso, 1986).<sup>1</sup> Capsaicin-produced desensitization was noticed to prevent neurogenic inflammatory responses caused by the application of nitrogen mustard (Carmas and Bito, 1980),<sup>2</sup> nicotine and acetylcholine (Jancso et al, 1961),<sup>3</sup> the electrical stimulation of the sensory nerves (Szolcsanyi, 1977 a, b),<sup>4,5</sup> or by orthodromic stimulation of pain sensitive nerve terminals with irritants (Jancso et al, 1967).<sup>6</sup>

Capsaicin was also known to produce hypothermia (Issekutz et al, 1950)<sup>7</sup> which was found to cause a fall in the metabolic rate (Issekutz et al, 1950 b<sup>8</sup>, Szulcsany, 1967).<sup>9</sup> And the administration of capsaicin in repetitive or high doses was found to cause desensitization to capsaicin's hypothermic action (Szolcsanyi, 1967<sup>9</sup>, Jansco-Gabor et al, 1970).<sup>10</sup>

Capsaicin was also reported to diminish the plasma extravasation response to histamine and bradykinin (Arvier et al, 1977,<sup>11</sup> Jansco et al, 1980<sup>12</sup>), and to result in a remarkable increase in gastric blood flow (Kolotat and Chungcharen, 1972,<sup>13</sup> Limlomwongse et al, 1979).<sup>14</sup>

Regarding the possible effects of capsaicin on the absorption or transport across biological membranes, it was found out that it alters the duodenal absorption of fats (Nopanitaya, 1973)<sup>15</sup> and inhibits the in vitro intestinal transport of glucose (Monsereenusorn and Glinsudon, 1978).<sup>16</sup>

Only very few works had been done regarding the possible effects of capsaicin on xenobiotics metabolism. It was reported to increase the microsomal P-450 (Kim et al, 1979).<sup>17</sup> Its reported effect on hexobarbital sleeping time in rats revealed a contradiction. In one of those reports, it was observed to prolong the sleeping time (Balint, 1972),<sup>18</sup> while in the other (Kim et al 1979),<sup>17</sup> capsaicin was shown to produce the reverse, i.e. a decrease in the sleeping time.

Some of the other effects of capsaicin that were pointed out in the literature by the end of 1970s, were its in vitro ability to labilize rat liver lysosomes (Smith et al, 1970),<sup>19</sup> to inhibit the Na<sup>+</sup> -K<sup>+</sup> -ATPase activity in the rat jejunum (Monsereenusorn and Glinsukon, 1979)<sup>20</sup> and to exert antibacterial effects against some microorganisms (Gal et al, 1968, 1969).<sup>21, 22</sup> In addition to that, capsaicin was even suspected, in an early report of the time (Hoch-Ligeti, 1951),<sup>23</sup> to be responsible for production of liver tumors in rats.

## IV. A review of our early findings

The performed studies may be classified into three major aspects:

- i. Studying the possible influence of capsaicin on experimental induction of peptic ulcer.
- ii. Studying the possible influence of capsaicin on drug absorption and transport across biological membranes.
- iii. Studying the possible effects of capsaicin in different test systems intended for exploring certain safety concerns.

Accordingly, the obtained findings will be presented in the following three sections:

### A. “The protective effect of capsaicin against experimental induction of gastric ulcers in rats”

The above-mentioned title was exactly the same one under which our work was presented, as a poster, at the international 41<sup>st</sup> FIP's congress in Vienna, in September 1981.

Certainly, there was an intention to formulate the presentation's title in such a direct way. The reason was simply that, at that time (1981), the general understanding (or belief), whether of the layman or even the scientists, was that capsaicin, as the active principle of hot pepper, constitutes a direct cause of induction of peptic ulcer. Meanwhile, we (as a small research team) had become highly convinced that this public understanding is nothing but a wrong COMMON SENSE, and that it is high time to report our findings to the scientific community.

In fact, this common sense was so strong that most of the scientists who looked at the poster did not hide their surprise and astonishment. In order to make it possible to realize the extent of surprise and astonishment that surfaced as a reflex to our work at that time (1981), we point to the following statement that was mentioned in a very recent publication:<sup>24</sup>

“The prevalent notion among a section of population in this country (India) and perhaps in others is that red pepper, a common spice, leads to “gastric ulcers” in view of its irritant and likely acid secretion nature. However, investigations carried out revealed that red pepper or its active principle, capsaicin, is not the cause for ulcer formation but ‘BENEFACTOR’.” [MN Satyanarayana, 2006].

Thus, if there is still a belief at 2006 that normal dietary ingestion of capsaicin (through hot pepper) causes peptic ulcer, and this even after the so many relevant research works have been conducted during the last few decades, then one can realize how deeply rooted this wrong common sense



was in 1981, and how the findings of our small research team were necessary in order to introduce a needed change.

What exactly were our findings? Were there any precedent findings that were similar and/or relevant in this context? And what was our explanation?

Actually, the communication that was presented at the FIP's international congress (1981), as documented in the abstract book,<sup>25</sup> showed that capsaicin protects against induction of gastric ulcer produced by two different experimental models in rats. The first model was the induction of gastric ulcer by prolonged forcible immobilization for 30 hours (Brodie et al, 1962<sup>26</sup> and Kandil and Gobran 1979).<sup>27</sup> It is denoted here as the "S-model". The other model, called the A-model, was that of aspirin administration (300mg/Kg) to pylorus ligated rats (Urishidani et al.).<sup>28</sup>

The taken criterion in the two models was the average number of ulcers per animal (Anichkov and Zavodskaya, 1968).<sup>29</sup>

In the two experimental models, the effect of capsaicin was tested through its oral administration, either in single or daily repetitive doses, before exposing the animal to induction of gastric ulcer.

On the one hand the utilized single doses of capsaicin, in the case of the S-model, were 1, 4 and 8mg/Kg, while the daily repetitive doses were 1, 2, and 4mg/Kg (for 7 days) or 2mg/Kg (for 14 days). On the other hand, only one single dose level of capsaicin (1mg/Kg) was utilized in the case of the "A-model", whereby two repetitive dose levels (2mg and 8mg/Kg) were applied for 30 days.

The obtained results showed that capsaicin decreased gastric ulceration by each of the two used models. Percentages of decrease in the number of gastric ulcers ranged between 13.33 and 80.55 in the single dose experiments. The maximum produced lowering in the incidence of gastric ulcers was produced by the single dose of 4mg/Kg in case of the S-model, and by that of 1mg/kg that was utilized in the case of the "A-model". The 7 days administration of capsaicin before exposure to stress resulted in dose-dependent reduction of the incidence of gastric ulcers, where the percentages of reduction were 30.75, 52.53, and 80.55 following the administered dose levels of 1, 2 and 4mg/Kg, respectively. When administering the dose of 2mg/Kg /day for 14 days, the reduction in the gastric ulcer incidence was 61.12%. The daily repetitive administration of 2 and 8mg/Kg of capsaicin before exposure to the "A-model" resulted in lowering the induction of gastric ulcers by 28.57% and 100% (i.e. full reduction), respectively.

The interpretation that the authors could propose at that time (1981) for the explored protective effect of capsaicin included two suggested mechanisms, namely the local hyperaemia and the desensitization of the sensory nerve endings. Later on, the two mechanisms were affirmed in more recent works while – also – other important mechanisms were explored.

### **B. The effect of capsaicin on drug absorption and transport across biological membranes**

The first reported finding indicating the potential of capsaicin as an enhancer of drug absorption was presented at the 8<sup>th</sup> International Congress of Pharmacology held in Tokyo in July 1981.<sup>29</sup>

This study was conducted on 22 volunteers who were themselves pharmacy students (18-22 years old). They were classified into two groups. Those who do not eat capsicum (6 students) are named “non-eaters”, and those who are used to eat it (16 students) are named “eaters”. The work utilized the model of buccal absorption that was introduced by Beckett and Triggs (1967).<sup>60</sup> The basis of the work was to assess the extent of buccal absorption of 10mg of sulfathiazole, in presence and in absence of a reasonable amount of capsaicin (0.024mg), during incubation of the drug solution in the buccal cavity for a short period (1 to 7 minutes). The obtained results showed that the “eaters” show significantly higher sulfathiazole absorption than those who do not eat capsicum, the “non-eaters”. Moreover, while the presence of capsaicin caused significant enhancement of drug absorption in both groups, the percentage of enhancement was much higher in the case of the non-eaters of capsicum. Therefore, the non-eaters of capsicum were found to be more sensitive to the enhancement of absorption by capsaicin.

The interpretation of the obtained results at that time included pointing to the observed higher enhancement of absorption in the non-eaters as an indication for the increase in blood flow as the main mechanism. This proposal was based on the already known property of capsaicin's desensitization of nerve endings following repetitive exposures to it.<sup>1</sup> Thus, the lesser degree of sensitivity of the eaters was associated with a lesser blood flow, and hence, a lower enhancement of absorption under influence of capsaicin. Also, another proposal was that the long-term use of capsicum as a spice (by the eaters group) may affect the membrane lining of the buccal cavity, where the effect may be a direct one (e.g. a cytotoxic effect) or an indirect one (e.g. an effect on blood flow).

The found enhancement of buccal absorption of sulfathiazole in healthy volunteers came in contradiction with the earlier reported finding of Monsereenusorn and Glinsukin<sup>16</sup> who reported that capsaicin inhibits the in-vitro transport of glucose across biological membranes. Thus, there was a need for further works to be done for the sake of exploration of more facts regarding our finding that capsaicin enhances drug absorption, and also regarding the contradiction with the above mentioned earlier report,<sup>16</sup> which was the only published one concerning the effect of capsaicin on transport of xenobiotics across biological membranes.

Accordingly, other studies were conducted in which the effect of capsaicin on drug absorption and transport across biological membranes was further explored. These studies included the effect on the in-vitro gastrointestinal absorption of each of sulfamethazine 30 and acetaminophen 31 in rats, the buccal absorption of glucose<sup>32</sup> in healthy volunteers, as well as the transport of glucose across (or into) the frog's skin.<sup>33</sup> All the findings of these studies, except that of acetaminophen, were presented at the 43<sup>rd</sup> International Congress of Pharmaceutical Sciences in Montreux, Switzerland (1983).

In the study of sulfamethazine sodium, each of the capsaicin and sulfamethazine were orally administered to adult rats in the dose levels 2mg/Kg and 80mg/Kg, respectively. The kinetics of absorption were assessed through the estimation of sulfamethazine in plasma along a period of 540 minutes. The obtained results indicated that capsaicin administration results in increasing each of the initial sulfamethazine plasma concentration (by 34.61%), the constant rate of absorption (by 75.59%) as well as the area under the plasma drug level (by 18.07%), while the constant rate of elimination was not affected. Thus, more evidence was produced regarding the enhancement of the absorption process by capsaicin.

Apart from that, there was a need to explore the case with glucose. The conducted study on the buccal absorption of glucose<sup>32</sup> utilized 3 concentrations of glucose (25, 50 and 100%) as well as 3 concentrations of capsaicin (0.5X, X and 2X, where X=0.096%). Three periods for the buccal incubation of the absorption of fluid were utilized, namely 3, 5 and 7 minutes. And the obtained results showed that capsaicin enhances the absorption of the three used concentrations of glucose, and that its effect (within the used range of concentrations) was concentration-dependent as the absorption increases with increasing capsaicin concentration.

There was a need to check the effect of capsaicin on the in-vitro glucose transport across (or into) biological membranes where there can be a possibility to investigate the effects of capsaicin in low as well as high

concentration. For this purpose, the transport across (or into) the frog's abdomen skin was utilized by using specially designed glass cells.<sup>33</sup> The site of transport was the internal surface of the skin. The experiments were conducted using 4 concentrations of glucose (50, 100, 300 and 600mg %) and 4 concentrations of capsaicin, namely 1X, 2X, 6X and 12X (where X=0.048 mg %). The obtained results showed that capsaicin enhances disappearance of glucose from the absorption site, and that its enhancement is dependent on the concentration of capsaicin where it was on the one hand progressively inhibited on increasing concentration from 1X up to 6X. On the other hand, the application of the highest used concentration of capsaicin (i.e. 12X) showed significant inhibition of the transport (or disappearance) of glucose.\*

Thus, taking into consideration that the utilized doses of capsaicin in our in-vitro studies were relatively low and close to the average range of the normal daily amounts ingested through meals, it was possible to conclude that proper doses of capsaicin enhance drug absorption and transport across biological membranes, and that an opposite effect may occur if capsaicin's concentration is high. In fact, the earlier reported inhibition of glucose transport under the influence of capsaicin (Monsereenusorn and Glinsukon, 1978) was the outcome of applying a capsaicin concentration that was about 24 times higher than the highest concentration used in our in-vitro experiments. Thus, it was possible to regard capsaicin's inhibitive effect on glucose transport as a consequence of its cyto-toxicity.

The increase of drug absorption under the influence of capsaicin was again confirmed through studying the acetaminophen gastrointestinal absorption in rats.<sup>31</sup> This study was conducted using the oral administration of 300mg/Kg of acetaminophen and 1 or 50mg/Kg of capsaicin. The obtained results showed that capsaicin administration results in increasing each of the initial plasma concentration, the constant rate of absorption as well as the area under the curve of plasma levels. The result was that either no, or only minimal additional effect was obtained by the 50-fold increase of the capsaicin dose. However, the administration of capsaicin was found to increase in a similar way the constant rate of elimination, an effect that was not found in the study of the gastrointestinal absorption of sulfamethazine in rats.<sup>30</sup> The proposed explanation was that capsaicin may increase the metabolism of acetaminophen, an explanation which may be

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\* *It must be frankly noticed here, after about 35 years of performing that experiment, that while it was too primitive, nevertheless, it served a lot in answering some of the arisen research questions in spite of the very limited technical facilities.*

supported by the finding that capsaicin is able to act as an enzyme inducer (Hamid et al, 1985).<sup>34</sup>

Regarding the effects of capsaicin on drug metabolism, two findings, contradictory to each other, had been reported, namely that capsaicin prolongs hexobarbital sleeping time, which may indicate an inhibition of drug metabolizing enzymes,<sup>18</sup> and that capsaicin decreases sleeping time, which indicates a stimulation of drug metabolizing enzymes. Our conducted experiments, regarding capsaicin and drug metabolism, indicated that capsaicin is able to activate the 4-hydroxylation of biphenyl in-vitro.<sup>35</sup> Following the daily subcutaneous administration of capsaicin (1 or 3mg/Kg) to rats for 3 days, the liver fractions showed an activation of the 4-hydroxylation of biphenyl, while no effect was shown regarding the 2-hydroxylation process.<sup>34</sup> The activation of the 4-hydroxylation process, in absence of cofactors, was shown to be dose-dependent, where the highest used dose of capsaicin produced 85.44% of that produced by phenobarbital (50mg/Kg, ip daily for 3days). In the same report, the single subcutaneous administration of 3mg/Kg of capsaicin to rats was shown to prolong the duration of hexobarbital sleeping time, while the daily repetitive administration for 3 days resulted in abolishing induction of sleep by the same dose of hexobarbital (65mg/Kg, ip).

Actually, this in-vivo study, regarding the effect of single and repetitive subcutaneous doses of capsaicin on the hexobarbital sleeping time, was conducted while the controversy between the findings of Balint (1972)<sup>18</sup> and those of Kin et al. (1979)<sup>17</sup> was in mind. The complete variation between the effects of the single and repetitive doses in our work<sup>34</sup> allowed the proposal that the prolongation of sleeping time under effect of the single dose of capsaicin may be due to its induced hypothermia which had been earlier reported to cause a decrease in the metabolic rate.<sup>7, 8, and 9</sup>

On the other hand, the desensitization to the hypothermic effect of capsaicin following its repetitive administration<sup>36</sup> may allow the induction of the drug metabolizing enzymes to be evident, with the consequence of shortening the sleeping period or abolishing it.

### **C. Exploration of certain safety concerns regarding the effects of Capsaicin**

These studies were conducted at the institute of Toxicology of the ETH and the University of Zurich (1983/84). They included the assessment of capsaicin regarding its possible mutagenicity and cytotoxicity, as well as its possible interference with osmotic fragility of red blood corpuscles, bleeding time and behaviour.

Regarding mutagenicity testing (Hamid et al., 1989),<sup>37</sup> the testing system was that of the Ames test. Eight concentrations of capsaicin (19.5-2500µg/plate) were subjected to the test, utilizing 5 strains of *Salmonella typhimurium* and 5 diagnostic mutagens. The experiments were conducted in presence and in absence of the so-called S-9 Fraction, i.e. the microsomal fraction of rat liver homogenate together with the essential co-factors, as a source of mammalian metabolic activation. The obtained results indicated the absence of any mutagenicity by capsaicin or its possible metabolites in the Ames testing system. They also showed that the high concentrations of capsaicin exert a toxic (bactericidal) effect on some of the tested strains, namely TA100, TA1537 and TA1358. These results confirmed those previously done by Buchanan et al. (1981)<sup>38</sup> which were conducted on only 3 *Salmonella typhimurium* strains.

Cytotoxicity of capsaicin was in-vitro evaluated by means of the cell detachment and cell growth assays (Hamed and Reinhardt)<sup>39</sup> using three cell lines, BHK-21/C13 (Baby hamster kidney cells), Keller cells (human diploid fibroblasts derived from an arm biopsy of an adult female) and MRC-5 cells (human embryonic lung fibroblasts). The obtained results showed a concentration-dependent detachment of cells where the percentages of detached cells have reached a maximum within a relatively narrow range of concentrations (0.2-2mM for MRC and BHK cells, and 0.2-0.6mM for Keller cells). Regarding the growth assay, significant inhibition occurred only at concentrations higher than 0.02mM. Thus, the produced growth inhibition may be just a consequence of cell detachment, where capsaicin was found to be a potent cell detaching agent that could be classified according to Reinhardt et al (1985)<sup>40</sup> as a strong cytotoxic agent. On the other hand, the exposure to capsaicin, whether in-vitro ( $10^{-4}$  to  $10^{-2}$  M) or in-vivo, either orally (5 or 50mg/Kg) or subcutaneously (1 or 3mg/Kg), did not affect osmotic fragility of red blood corpuscles in rats as indicated by the mean corpuscular fragility (MCF). Here, it should be emphasized that the utilized high oral dose is about 50 times the assumed average of daily consumption for man (Monseernusorn et al, 1982)<sup>41</sup>, and that the given subcutaneous dose allowed the escape of the first-pass effects, if any. In addition, the highest utilized in-vitro concentration had resulted in super saturation of the test solution.

Accordingly, capsaicin is not liable to affect the red blood corpuscles membrane in man. The performed studies were extended to evaluate the effects of capsaicin on the bleeding time<sup>42</sup> where a significant prolongation was observed. The performed evaluation of the possible effect of capsaicin on behaviour was performed on the locomotor activity of rats by using the residential maze technique.<sup>43</sup> Capsaicin was found not to interfere with the