NATURAL PRODUCTS:
Research Reviews

— Volume 4 —

The Editor

Dr. Vijay Kumar Gupta, Ph.D., FLS, London (born 1953-) Ex. Chief Scientist, CSIR- Indian Institute of Integrative Medicine, Jammu, India. He did his M.Sc. (1975) and Ph.D. (1979) in Zoology both from University of Jammu, Jammu-India. His research capabilities are substantiated by his excellent work on histopathology, ecology and reproductive biology of fishes, turtles, birds and mammals, which has already got recognition in India and abroad.

Dr. Gupta has to his credit more than 150 scientific publications and review articles which have appeared in internationally recognized Indian and foreign journals. Founder fellow, life member and office bearer of many national societies, academies and associations. He has successfully completed a number of research/consultancy projects funded by government, private and multinational agencies. His current areas of interest are histopathology, toxicology, pre-clinical safety pharmacology, reproductive efficacy studies of laboratory animals and biodiversity.

He is the Series Editor of the recently published multi-volume set of books, "**Comprehensive Bioactive Natural Products (Vols. 1-8)"**, published by M/S Studium Press, LLC, USA. He is also Editor-in-Chief of the books, "**Utilisation and Management of Medicinal Plants (Vols. 1-3)"**, "**Medicinal Plants: Phytochemistry, Pharmacology and Therapeutics (Vols. 1-4)", "Traditional and Folk Herbal Medicine (Vols. 1-3)"** , **"Natural Products: Research Reviews (Vols. 1-4)", "Bioactive Phytochemicals: Perspectives for Modern Medicine (Vols. 1-3)", "Perspectives in Animal Ecology and Reproduction (Vols. 1-10**)" and **"Animal Diversity, Natural History & Conservation (Vols. 1-5)"**. The Editor-in-chief of the American Biographical Institute, USA, has appointed him as *Consulting Editor* of *The Contemporary Who's Who*. Dr. Gupta also appointed as Nominee for the *Committee for the Purpose of Control and Supervision of Experiments on Animals* (CPCSEA, Govt. of India). The *Linnaean Society of London, U.K.* has awarded fellowship to him in November 2009 in recognition of his contribution towards the cultivation of knowledge in Science of Natural History. Recently, Modern Scientific Press, USA has nominated Dr. Gupta as the Editor of the *International Journal of Traditional and Natural Medicine*.

NATURAL PRODUCTS:
Research Reviews

— Volume 4 —

Editor
V.K. Gupta
Chief Scientist (Ex)
CSIR-Indian Institute of Integrative Medicine
Canal Road, Jammu – 180 001,
India

2016
Daya Publishing House®
A Division of
Astral International Pvt. Ltd.
New Delhi – 110 002

Cataloging in Publication Data--DK
Courtesy: D.K. Agencies (P) Ltd. <docinfo@dkagencies.com>

Natural products : research reviews / editor, V.K. Gupta.
volume 4 cm
Includes bibliographical references and index.

ISBN 978-93-5124-686-2 (Hardbound)
ISBN 978-93-5130-883-6 (International Edition)
ISBN 978-81-7035-774-2 (Series)
ISBN 978-93-5130-104-2 (Series) (International Edition)

1. Natural products. 2. Botanical chemistry. 3. Materia medica, Vegetable. I. Gupta, V. K. (Vijay Kumar), 1953- editor.

QK861.N38 2016DDC 572.2 23

Published by : **Daya Publishing House®**
A Division of
Astral International Pvt. Ltd.
– ISO 9001:2008 Certified Company –
4760-61/23, Ansari Road, Darya Ganj
New Delhi-110 002
Ph. 011-43549197, 23278134
E-mail: info@astralint.com
Website: www.astralint.com

Laser Typesetting : **Classic Computer Services,** Delhi - 110 035

Printed at : **Thomson Press India Limited**

PRINTED IN INDIA

Editorial Board

Prof. Ian Fraser Pryme

Department of Biomedicine,
University of Bergen,
Jonas Lies vei 91, N-5009 Bergen, NORWAY
Tel: +47-55-586438
Fax: +47-55-586360
E-mail: ian.pryme@biomed.uib.no

Dr. George Qian Li

Herbal Medicines Research and Education Centre,
Faculty of Pharmacy, The University of Sydney,
NSW 2006, AUSTRALIA
Tel: 612 9351
Fax: 9351 8638
E-mail: george.li@sydney.edu.au

Dr. Julia Serkedjieva

Institute of Microbiology,
Bulgarian Academy of Sciences,
26, Academician Georgy Bonchev St.,
1113 Sofia, BULGARIA
Tel: +359 2 979 31 85
Fax: +359 2 870 01 09
E-mail: jserkedjieva@microbio.bas.bg

Centro de Investigação em Ciências da Saúde
Health Sciences Research Centre

UNIVERSIDADE DA BEIRA INTERIOR
Faculdade de Ciências da Saúde

Foreword

Nature is a vast and almost infinite source of new bioactive compounds and has been the source of traditional medicine for thousands of years. Natural products are in the origin of important modern drugs and continue being an essential partner in drug discovery. The search for bioactive natural products in order to discover new drugs has a long tradition and over the last years there has been a renewed interest in natural products research, looking for alternative drugs for key therapeutic areas such as cancer and infectious diseases. More recently bioactive compounds from natural sources have been widely used in cosmetics and as health supplements. Persistent research in natural products is needed to find new lead drugs and to continue to be competitive. This book provides the latest evidences supporting the progress of this research. The book exhibits a total of 22 chapters authored by scientists from across the world and representing different scientific disciplines, bringing different approaches of natural products research and showing the multidisciplinary of this type of research.

Some chapters are devoted to the review of chemical, nutritional and pharmacological of several plants, including *Camellia sinensis*, *Prunus avium*, *Alpinia* spp., *Achilla millefolium*, *Hypericum* spp., *Oroxylum indicum*, *Hemidesmus indicus*, *Codiaeum variegatum*, *Pterocarpus marsupium*, *Digera muricata*, *Smilax chinensis*, as well as of marine derived products. Different plant pharmacological properties, including anticancer, treatment of sexual dysfunctions, management of anxiety disorders, genotoxicity and genoprotection and diabetic wound healing, have been covered in the book. Biotechnological and technological applications of natural products in drug delivery systems, as well as the use of plants to synthesize nanoparticles, were also reviewed in other chapters.

Av. Infante D. Henrique, 6200-506 Covilhã, PORTUGAL
Telef.: +351 275 329 002 | Fax: +351 275 329 099
e-mail: fcsaude@fcsaude.ubi.pt | www.ubi.pt

Overall, we hope that this fourth volume of *Natural Products: Research Review* edited by Dr. V.K.Gupta constitutes an elucidative state of the art about some hot topics in the growing areas of Pharmacognosy, Phytotherapy and Drug Development. We expect that the content of this book will be a source of inspiration for future developments in these fields and we hope that readers will find it a useful and functional tool in natural products research.

Ana Paula Duarte, PhD

Branca M. Silva, PhD

Health Sciences Research Center, CICS-UBI

Faculty of Health Sciences, University of Beira Interior, Covilhã, Portugal

Preface

Drug discovery in ancient times was largely by chance and based on clinical practices. As understanding of therapeutic benefits deepens and demands for natural products increase, previously serendipitous discoveries evolved into active searches for new medicines. Natural Products offer a vast, virtually untapped reservoir of chemical compounds with many potential uses, which have been described along with well illustrated structural form elucidation. Despite the enormous potential, only a minor fraction of globe's living species has ever been tested for any bioactivity. For instance, approximately only 10 per cent of all existing plant species has been assayed, and in the case of microbes the value is even lower.

Natural products are organic molecules isolated from animals, plants, or microbes that can be used to treat human disease. Through evolutionary pressure, nature has guided the production of an immense diversity of organic molecules for a variety of biological purposes. In order to search natural sources for new therapeutics, generally crude fractions of biological material are screened for biological activity. Fractions with activity are further purified and retested until the bioactive natural product is identified. Natural product preparations have historically been the major source of pharmaceutical agents. Bioactive natural products have a range of potential applications, including pharmaceuticals, dietary supplements, and controls agents for crop pests and diseases. Extracts and biomolecules with promising activity are unscrupulously screened for efficacy to determine if these products have a potential for commercial development.

There is a revival of interest in the use of natural products in pharmacy, both from the pharmaceutical industry as a source of new lead molecules and from the general public who are using natural extracts in many ways in conventional and complementary therapies. Analysis of FDA new-drug approvals from 1981 to 2002 reveals that natural products continued to play a pivotal role during that time, even if the industry had turned to other discovery strategies. Indeed, more than 90 per cent of current therapeutic classes derive from a natural product prototype and interestingly,

even today, roughly two-thirds to three quarters of the world's population relies upon medicinal plants for its primary pharmaceutical care (World Health Organization, 2002). Those "medicinal plants" are either preparations of or natural product substances from plants that have potential utility as pharmaceutical agents.

It is for their world wide a sustained effort of scientist's that enormous information is being generated and there has been a series of publications on natural products researches. Based on this rational, the present volume **"***Natural Products: Research Reviews Vol. 4*" presents information on review communications received from eminent scientists from India and abroad, providing recent and present state of the art data on therapeutic properties, action and uses of bioactive natural products in combating a number of diseases and condition for which there is lesser satisfactory treatment in modern medicine.

V.K. Gupta

Contents

Natural Products: Research Reviews Vol. 4 (2016) *Pages* **21–62**
Editor: **V.K. Gupta**
Published by: **DAYA PUBLISHING HOUSE, NEW DELHI**

2

Camellia sinensis (L.) Kuntze: A Review of Chemical and Nutraceutical Properties

Ana Paula de Oliveira[1], Amanda Leite Guimarães[1],
Raimundo Gonçalves de Oliveira-Júnior[1],
Jullyana de Souza Siqueira Quintans[2],
Fernando Antônio de Medeiros[3], José Maria Barbosa-Filho[4],
Lucindo José Quintans-Júnior[2] and
Jackson Roberto Guedes da Silva Almeida[1]*

ABSTRACT

The tea plant Camellia sinensis (L.) Kuntze (family Theaceae) is grown in about 30 countries worldwide. Tea, known as the most popular beverage on Earth, arouses great interest among scientists due to its beneficial health effects. There are numerous studies about the composition of C. sinensis demonstrating that tea contains purine alkaloids (xanthines), phenolic compounds (catechins, O-glycosylated flavonols, C-glycosylated flavones, proanthocyanidins and phenolic acids and their derivatives), terpenoids, fatty acids, essential oils and amino acids. Tea flavonoid consumption has been linked to lower incidences of chronic diseases such as cardiovascular disease and cancer. For this review, the search was carried out using Web of Science, Chemical Abstracts and the data bank NAPRALERT (acronym for NAtural PRoducts ALERT), updated from January 2000 to July 2013. The references

1 Center of Studies and Research of Medicinal Plants, Federal University of San Francisco Valley, 56.304-205, Petrolina, Pernambuco, Brazil.

2 Department of Physiology, Federal University of Sergipe, 49.000-100, São Cristóvão, Sergipe, Brazil.

3 Federal University of Amapá, 68.902-280, Macapá, Amapá, Brazil.

4 Federal University of Paraíba, 58.051-970, João Pessoa, Paraíba, Brazil.

* *Corresponding author*: E-mail: jackson.guedes@univasf.edu.br

found in the search were then studied in detail. The review refers to 83 compounds isolated from C. sinensis, which are classified in appropriate chemical groups. Some aspects of bioactivity of the secondary metabolites produced are discussed. For this purpose, 165 references were consulted.

Keywords: *Camellia sinensis*, Tea, Phytochemistry, Pharmacology, Nutraceutical, Antibacterial, Anti-inflammatory, Antioxidant, Anticancer, Anticarcinogenic, Anti-diabetic, Cytotoxic, Hepatoprotective, Hypocholesterolemic, Neuroprotective.

Introduction

The tea plant *Camellia sinensis* (L.) Kuntze (family Theaceae) is grown in about 30 countries worldwide (Graham, 1992). It grows best in tropical and subtropical areas with adequate rainfall, good drainage and slightly acidic soil (Graham, 1999). There are two varieties of tea. *C. sinensis* var. *sinensis* (China tea) is grown extensively in China, Japan and Taiwan, while *C. sinensis* var. *assamica* (Assam tea) predominates in South and Southeast Asia, including Malaysia (Adiwinata *et al*., 1989). Figures 2.1A and B shows the leaves of the plant *C. sinensis* commonly used in the production of tea.

Tea is one of the most widely consumed beverages in the world. *C. sinensis* has been used for tea beverage since 3000 B.C. consisting of the leaf and bud of the plant *Camellia sinensis*. Also, it is the oldest non-alcoholic beverage in the world, having been consumed socially and habitually for several years (Mondal *et al.,* 2004). Recent epidemiological studies suggest that green tea has diverse biological activities, including antioxidant, antimutagenic, anticarcinogenic, antibacterial, antiviral and anti-fibrotic activities. In addition, it has been shown to alleviate the symptoms of hypertension, reduce the risk of cardiovascular disease, improve oral health, protect against solar ultraviolet radiation, control body weight, improve glucose tolerance and insulin sensitivity, increase bone mineral density, and maintain neuroprotective activity (Cabrera *et al.,* 2006). A recent study has suggested that green tea extract is safe as a dietary supplement and has many properties that are beneficial for human health (Frank *et al.,* 2009).

Tea is the most widely consumed beverage in the world, second only to water. The amount of consumption well exceeds coffee, beer, wine and soft drinks. There are three kinds of teas obtained from *Camellia sinensis* plant: not fermented (green and white tea), partially fermented (red and oolong tea) and completely fermented (black tea), and their compositions are affected by the fermentation process. Figure 2.2 shows the processing steps for some of the different types of tea obtained from *C. sinensis* (Paganini-Costa and Carvalho-da-Silva, 2011). Of the total amount of tea produced and consumed in the world, 78 per cent is black, 20 per cent is green and 2 per cent is oolong tea. In green tea manufacturing, catechin oxidation by polyphenol oxidase is prevented by steaming (Japan) or by panning (China) (Graham, 1999). The leaves retain their green color and almost all of their original polyphenol content. Oolong tea is allowed to ferment to a limited extent and contains a mixture of catechins,

Figure 2.1: *Camellia sinensis* (L.) Kuntze Standing Crop (A) and Close Up of Leaves (B) (Photo courtesy: S. K. Basu, Lethbridge, AB, Canada).

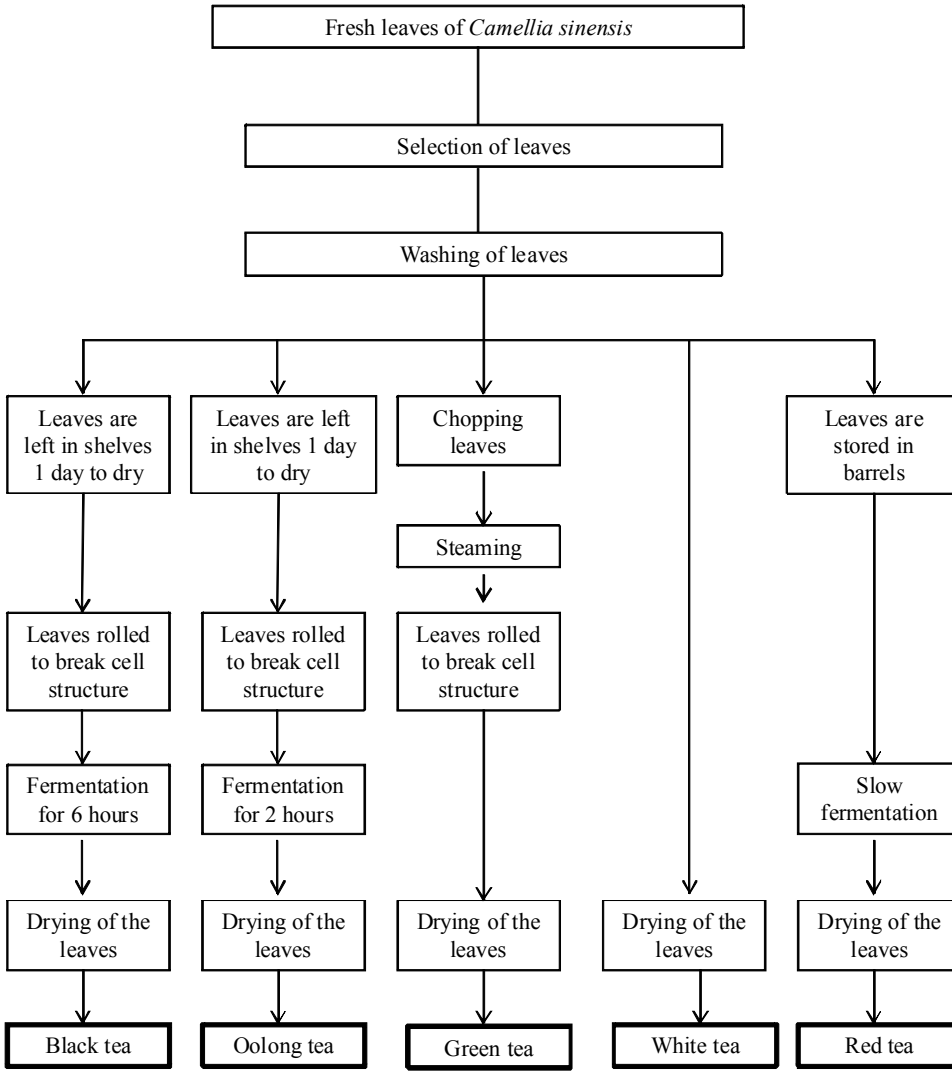


Figure 2.2: Processing Steps for some of the different Types of Tea obtained from *C. sinensis*.

theaflavins and thearubigens. Black tea is produced from fully fermented leaves and has a characteristic color and taste (Chan *et al.*, 2007).

To produce green tea, the young leaves are rolled and steamed to minimize oxidation. In the production of black tea, after the leaves are rolled, which disrupts cellular compartmentation and brings phenolic compounds into contact with polyphenol oxidases, the young *C. sinensis* leaves undergo oxidation (referred to as fermentation) for 6 hours. During this period, catechins are converted to complex condensation products, the theaflavins and their polymers, thearubigins. Oolong tea

is produced with a shorter fermentation period than black tea and has a taste and color somewhere between green and black teas. White tea is prepared from very young tea leaves or buds covered with tiny, silvery hairs, which are harvested only once a year in the early spring. White tea is steamed and dried immediately after picking to prevent oxidation, giving it a light, delicate taste. In spite of numerous data about the phenolic constituents, antioxidant activity and ameliorating effects of green and black tea on human health, little is known in this sense about white tea, which is the rarest and the least processed tea (Rusak *et al.,* 2008).

Even today, the chemical composition of *C. sinensis* has been explored, and novel compounds are continuously discovered. Polyphenols constitute the most interesting group of green tea leaf components, and in consequence, green tea can be considered an important dietary source of polyphenols, particularly flavonoids (Cabrera *et al.,* 2006). Catechins are the major flavonoids present in green tea. The four principal catechins are (-)-epigallocatechin-3-gallate (EGCG), that represents approximately 59 per cent of the total catechins; (-)-epigallocatechin (EGC) (19 per cent approximately); (-)-epicatechin-3-gallate (ECG) (13.6 per cent approximately); and (-)-epicatechin (EC) (6.4 per cent approximately) (Soares *et al.,* 2013).

Phenolic flavan 3-ols in fresh tea leaf are transformed into two principal groups of phenolic pigments (red-orange colored theaflavin and rusty-red colored thearubigin) in black tea by fermentation, which is a natural browning reaction initiated by an oxidative enzyme (polyphenol oxidase) within the plant cell. Semi-fermented oolong tea is generally fermented from 20-60 per cent to avoid green tea's characteristic leafy and grassy notes while obtaining black tea's sweet and bold flavor. Oolong tea was traditionally reported to have anti-obesity and hypolipidemic effects coming from unoxidised tea catechins and oxidized theaflavins and thearubigins present in oolong tea. The data suggested that fermentation diminished antioxidant capacity of tea and could result in lowering potential health benefits from flavonoids. This result should be considered for tea manufacturing and the development of functional foods desiring maximum potential health benefits from antioxidant flavonoids in tea (Kim *et al.,* 2011).

White tea is very similar to green tea, but it is exceptionally prepared only from the buds and young leaves of *C. sinensis* plant, which are plucked only during the early spring before the buds have been fully opened. On the other hand, green tea is prepared from the matured tea leaves of the same plant. Several types of bioactive compounds are found in white tea such as polyphenols, caffeine, theogallin, gallic acid, theaflavin, flavonol glycosides and catechins, particularly epigallocathechins, epigallocatechins gallate, epicatechin gallate and epicatechin gallate. The concentrations of tea polyphenols, catechins and corresponding antioxidant activities are higher in white tea compared to green- or black tea. It was also reported that the concentrations of total polyphenols, total catechins, caffeine and epigallocatechin gallate are significantly higher in the white tea compared to green tea while only epigallocatechin and flavanol glycosides are higher in green tea compared to white tea (Islam, 2011).

The reasons for the worldwide popularity of tea were unique aroma and characteristic flavor, but recently, its popularity has increased due to its potential health benefits against cardiovascular diseases and cancer as well as pharmaceutical activities such as antihypertensive, antiateriosclerotic, hipocholesterolemic and hypolipidemic properties mostly from activities of antioxidant flavonoids present in tea. Monomeric flavonoids (flavan 3-ols or tea catechins) present in *C. sinensis* leaf are transformed to polymeric theaflavin and thearubigin by oxidation occurring during tea fermentation. The distinctive color, decreased bitterness and astringency and characteristic flavor are derived from the fermentation process giving fermented teas a marked distinction from non-fermented green tea. Even though teas are available in many different fermentation levels from green to black, the difference in phytochemicals and volatile compounds in tea with different degrees of fermentation has not been fully investigated yet within the same tea leaf (Kim *et al.*, 2011).

A number of studies during the last decade have linked tea consumption, especially green tea, to a reduced risk for cancer in humans, leading to increased popularity and credibility of tea as a healthy drink with chemopreventive properties (Blot *et al*., 1997). It has widely been accepted that drinking green tea is associated with a low incidence of human cancer (Uesato *et al.*, 2001). Since Higginson (1966) first published the epidemiological report on tea and cancer, many extensive studies about the chemopreventive efficacy of green tea against various types of cancer, including esophagus, breast, pancreas, prostate and colon cancer, have been carried out (Wei *et al.*, 2011).

Considering the importance of the species *Camellia sinensis* in the treatment of several diseases, especially diabetes, cardiovascular diseases and cancer, this chapter is a review of chemical and nutraceutical aspects of this species. We do not intend to conduct a comprehensive review of the literature, but rather to present introductory information on the subject. For more details about the properties of tea, the reviews of Pastore and Fratellone (2006), Yang *et al.* (2007) and Sharangi (2009) could be consulted.

Methods

A literature search on the biological activities of extracts and the presence of compounds in *C. sinensis* was carried out. The keywords used for the literature search for this review were *Camellia sinensis*, Theaceae, biological activity, medicinal plants and natural products. The search was carried out using Web of Sciences, Chemical Abstracts and the data bank NAPRALERT (acronym for NAtural PRoducts ALERT), updated January 2000 to July 2013. The references found in the search were then studied in detail.

Results and Discussion

In this section we present some considerations about extracts and chemical constituents of *C. sinensis* with biological activity. Consultation of various literature sources resulted in the elaboration of a list of some active extracts and preparations as well as chemical constituents isolated from *C. sinensis* (Tables 2.1 and 2.2). It should be noted that most of the references cited are not first-hand observations, but

Table 2.1: Biological Activities for extracts of *C. sinensis*.

Activity	*Extract/Preparation*	*Organism/Model*	*Results*	*Reference*
Acid phosphatase inhibition	H_2O extract	Rat (Ovariectomized)	Active	(Das *et al.,* 2005)
Agiogenesis inhibition	Decoction	Cell culture	Active	(Kojima-Yuasa *et al.,* 2003)
Alcohol dehydrogenase inhibition	Catechins and flavonoids	Yeast	Active	(Manir *et al.,* 2012)
Aldosterone agonist activity	Infusion	Human adult	Inactive	(Duffy *et al.,* 2001)
Analgesic activity	MeOH-H_2O (1:1) extract	Mouse	Active	(Chattopadhyay *et al.,* 2004)
Antiatopic dermatitis activity	Hot H_2O extract	Human adult	Active	(Uehara *et al.,* 2001)
Angiotensin converting enzyme stimulation	Hot H_2O extract	Cell culture	Inactive	(Melzig and Janka 2003)
Antibacterial activity	Ethyl acetate extract	Cell culture	Active	(Chauhan *et al.,* 2013)
	Ethanolic extract	Cell culture	Active	(Chauhan *et al.,* 2013)
	Methanolic extract	Cell culture	Active	(Chauhan *et al.,* 2013)
	H_2O:MeOH (60:40) extract	Cell culture	Active	(Chauhan *et al.,* 2013)
	Aqueous extract	Cell culture	Active	(Sharma *et al.,* 2012)
	Polyphenolic fraction	Human adult	Active	(Hirano *et al.,* 2002)
	Hot H_2O extract	*Staphylococcus aureus*	Inactive	(Yildirim *et al.,* 2000)
	Hot H_2O extract	*Pseudomonas aeruginosa*	Inactive	(Yildirim *et al.,* 2000)
	Hot H_2O extract	*Escherichia coli*	Inactive	(Yildirim *et al.,* 2000)
	Hot H_2O extract	*Bacillus subtilis*	Inactive	(Yildirim *et al.,* 2000)
	Infusion	*Staphylococcus aureus*	Active	(Sharquie *et al.,* 2000)
	Infusion	*Streptococcus pyogenes*	Active	(Sharquie *et al.,* 2000)
	Infusion	Human adult	Active	(Sharquie *et al.,* 2000)
	Infusion	Agar plate	Active	(Sharquie *et al.,* 2000)
	Infusion	*Helicobacter pylori*	Active	(Yee and Koo 2000)

Contd...

Table 2.1–*Contd...*

Activity	*Extract/Preparation*	*Organism/Model*	*Results*	*Reference*
Anti-diabetic activity	Aqueous extract	Rat	Active	(Islam 2011)
	Infusion	Rat	Active	(Abeywickrama *et al.,* 2011)
	Polyphenolic fraction	Rat	Active	(Sabu *et al.,* 2002)
Antidiarrheal activity	Decoction	Mouse male	Active	(Besra *et al.,* 2003)
	Decoction	Rat male	Active	(Besra *et al.,* 2003)
Antifibrotic activity	Phenolic fraction	Mice	Active	(Tsai *et al.,* 2013)
Antigastritis activity	Infusion	Human adult	Active	(Yu *et al.,* 2001)
Antigen expression enhancement	Phenolic fraction	Cell culture	Active	(Abou *et al.,* 2001)
Antihemolitic activity	Methanolic extract	Cell culture	Active	(Costa *et al.,* 2009)
Antihepatotoxic activity	Infusion	Rat male	Active	(Altiner and Yenice 2000)
	Polyphenolic fraction	Rabbit	Active	(Dou *et al.,* 2000)
	Flavonoid fraction	Mouse	Active	(Rao *et al.,* 2000)
Antihypercholesterolemic activity	Infusion	Human adult	Active	(Maron *et al.,* 2003)
	Infusion	Rat male	Active (Liver)	(Yang and Koo 2000)
	Infusion	Rat male	Active (Serum)	(Yang *et al.,* 2000)
Antihyperglycemic activity	H_2O extract	Human adult	Active	(Hosoda *et al.,* 2003)
Anti-inflammatory activity	MeOH-H_2O (1:1) extract	Rat	Active	(Chattopadhyay *et al.,* 2004)
	Infusion	Rat male	Active	(Das *et al.,* 2002)
	Infusion	Human adult	Active	(Krahwinkel and Willers-hausen 2000)
	Saponin fraction	Rat	Active	(Chaudhuri *et al.,* 2001)
Anti-ischemic effect	EtOH (70 per cent) extract	Gerbil female	Active	(Honh *et al.,* 2001)
	Chromatographic fraction	Rat	Active	(Honh *et al.,* 2000)

Contd...

Table 2.1–*Contd...*

Activity	*Extract/Preparation*	*Organism/Model*	*Results*	*Reference*
Antimutagenic activity	Aqueous extract	Cell culture	Active	(van der Merwe 2006)
	H_2O soluble fraction	Mouse male	Active	(Shukla and Taneja 2001)
	Hot H_2O extract	Mouse	Weak activity	(Krul *et al., et al.*, 2001)
	Hot H_2O extract	Mouse male	Active	(Jiang *et al.,* 2001)
	Hot H_2O extract	Cell culture	Active	(Steel *et al.,* 2000)
	Polyphenolic fraction	Cell culture	Active	(Steel *et al.,* 2000)
	$CHCl_3$ extract	–	Active	(Higashimoto *et al.,* 2000)
	Hot H_2O extract	Mouse female	Active	(Pressentin *et al.,* 2001)
Anti-obesity	Methanolic extract	Mice	Active	(Hamao *et al.,* 2011)
Antioxidant activity	Ethyl acetate extract	–	Active	(Chauhan *et al.,* 2012)
	Ethanolic extract	–	Active	(Chauhan *et al.,* 2012)
	Methanolic extract	–	Active	(Chauhan *et al.,* 2012)
	H_2O:MeOH (60:40) extract	–	Active	(Chauhan 2012)
	Polyssacharide fraction	Cell culture	Active	(Xu *et al.,* 2012)
	Methanol extract	–	Active	(Chan *et al.,* 2007)
	Polyphenolic fraction	–	Active	(Levites *et al.,* 2002)
	Hot H_2O extract	Rat male	Active	(Fadhel and Amran 2002)
	Decoction	Rat male	Active (Liver)	(Alessio *et al.,* 2002)
	Decoction	Rat male	Active (Kidney)	(Alessio *et al.,* 2002)
	Infusion	–	Active	(Nakagawa *et al.,* 2002)
	Hot H_2O extract	–	Active	(Krul *et al.,* 2001)
	EtOH-H_2O (50 per cent) extract	–	Weak activity	(Chung *et al.,* 2001)

Contd...

Table 2.1–*Contd...*

Activity	*Extract/Preparation*	*Organism/Model*	*Results*	*Reference*
	EtOH (70 per cent) extract	Gerbil female	Active	(Hong *et al.,* 2001)
	Infusion	Human adult	Active	(Chung *et al.,* 2001)
	Chromatographic fraction	Rat	Active	(Hong *et al.,* 2000)
	Tannin fraction	Cell culture	Inactive	(Yokozawa *et al.,* 2000)
	Infusion	Human adult	Active	(Langley-Evans *et al.,* 2000)
Antiproliferation activity	Hot H_2O extract	Cell culture	Active	(Melzig *et al.,* 2003)
Antiproliferation activity	Catechin fraction	Cell culture	Active	(Chung *et al.,* 2001a)
	Infusion	Rat male	Active	(Zhang *et al.,* 2000)
Antipyretic activity	MeOH-H_2O (1:1) extract	Rat	Active	(Chattopadhyay *et al.,* 2004)
	MeOH-H_2O (1:1) extract	Mouse	Active	(Chattopadhyay *et al.,* 2004)
Anti-stroke activity	Infusion	Human adult	Inactive	(Peters *et al.,* 2001)
Antitumor activity	Polyssacharide fraction	Cell culture	Active	(Xu *et al.,* 2012)
	Decoction	Hamster male	Active	(Li *et al.,* 2002)
	Infusion	Mouse male	Active	(Das *et al.,* 2002)
	Decoction	Mouse	Active	(Gupta *et al.,* 2001)
	Infusion	Mouse	Active	(Suganuma *et al.,* 2001)
Antiulcer activity	Decoction	Gerbil male	Active	(Matsubara *et al.,* 2003)
Antiyeast activity	EtOH (100 per cent) extract	*Candida albicans*	Active	(Vaijayanthimala *et al.,* 2000)
	H_2O extract	*Candida albicans*	Inactive	(Vaijayanthimala *et al.,* 2000)
	Hot H_2O extract	*Candida albicans*	Inactive	(Yildirim *et al.,* 2000)
	Saponin fraction	*Zygosaccharomyces roux*	Active	(Tomita *et al.,* 2000)
Aphrodisiac effects	Black tea brew	Rat male	Active	(Ratnasooriya and Fernando 2008)

Contd...

Table 2.1–*Contd...*

Activity	*Extract/Preparation*	*Organism/Model*	*Results*	*Reference*
Apoptosis induction	Root extract	Cell culture	Active	(Ghosh *et al.,* 2006)
	Infusion	Mouse	Active	(Bhattacharyya *et al.,* 2003)
	Decoction	Mouse	Active	(Gupta *et al.,* 2001)
	Catechin fraction	Cell culture	Active	(Chung *et al.,* 2001)
	Infusion	Cell culture	Active	(Zhang *et al.,* 2000)
	Catechin fraction	Cell culture	Weak activity	(Liu *et al.,* 2000)
	Polyphenolic fraction	Cell culture	Weak activity	(Hibasami *et al.,* 2000)
Apoptosis inhibition	EtOH (70 per cent) extract	Gerbil female	Active	(Hong *et al.,* 2001)
	Chromatographic fraction	Rat	Active	(Hong *et al.,* 2000)
Autophosphorylation inhibition	Polyphenolic fraction	Cell culture	Active	(Klein and Fischer 2002)
Blood alcohol level decreased	Type extract not stated	Mouse	Active	(Mao and Yu 2000)
Calcium level decrease	Catechin fraction	–	Active	(Kang *et al.,* 2001)
Carcinogenesis inhibition	Infusion	Mouse female	Active	(Shukla *et al.,* 2002)
Carcinogenesis inhibition	Type extract not stated	Rat male	Active (Liver)	(Zhang *et al.,* 2002)
Carcinogenesis inhibition	Lyophilized extract	Mouse female	Active	(Lu *et al.,* 2001)
	Hot H_2O extract	Mouse	Inactive	(Hebert *et al.,* 2001)
	Infusion	Human adult	Active	(Yu *et al.,* 2001)
	Infusion	Rat male	Active	(Qin *et al.,* 2000)
	Infusion	Rat male	Active	(Jia and Han 2000)
	Pigment	Rat male	Active	(Gong *et al.,* 2000)
	Polyphenolic fraction	Rat male	Active	(Gong *et al.,* 2000)
	Infusion	Rat male	Active	(Metz *et al.,* 2000)

Contd...

Table 2.1–*Contd...*

Activity	*Extract/Preparation*	*Organism/Model*	*Results*	*Reference*
Cardiotonic effect	Infusion	Human adult	Active	(Hodgson *et al.,* 2001)
Cariostetic effect	Infusion	Rat	Active	(Hamilton-Miller *et al.,* 2001)
	Not stated	Human child	Active	(Hamilton-Miller *et al.,* 2001)
	Infusion	Hamster	Active	(Hamilton-Miller *et al.,* 2001)
Caspase-3 stimulation	Infusion	Cell culture	Active	(Kennedy *et al.,* 2001)
Cell adhesion inhibition	Not stated	Cell culture	Active	(Xuan *et al.,* 2001)
Cell proliferation inhibition	H_2O extract	–	Active	(Dulloo *et al.,* 2000)
Cholesterol absorption inhibition	Infusion	Rat	Active	(Loest *et al.,* 2002)
Cyclooxigenase-1 inhibition	Infusion	Rat male	Inactive	(Metz *et al.,* 2000)
Cyclooxigenase-2 inhibition	Infusion	Rat male	Active	(Metz *et al.,* 2000)
Cytochrome C release stimulation	Infusion	Cell culture	Active	(Kennedy *et al.,* 2001)
Cytochrome P_{450} inhibition	Hot H_2O extract	Cell culture	Weak activity	(Greenblatt *et al.,* 2006)
Cytochrome P_{450} inhibition	Type extract not stated	Human adult	Inactive	(Donovan *et al.,* 2008)
	Hot H_2O extract	Rat female	Inactive	(Maliakal *et al.,* 2001)
Cytochrome P_{450} stimulation	Hot H_2O extract	Rat female	Active	(Maliakal *et al.,* 2001)
Cytotoxic activity	Root extract	Cell culture	Active	(Ghosh *et al.,* 2006)
	EtOH (60 per cent)	Cell culture	Inactive	(Bedoya *et al.,* 2002)
	Hot H_2O extract	Cell culture	Active	(Sartippour *et al.,* 2002)
Degranulation inhibition	Polyphenolic fraction	Cell culture	Active	(Tachibana *et al.,* 2000)
DNA adduct formation inhibition	Polyphenolic fraction	Cell culture	Active	(Steel *et al.,* 2000)
	Hot H_2O extract	Cell culture	Active	(Steel *et al.,* 2000)
DNA damage prevention activity	Infusion	Cell culture	Active	(Thiagarajan *et al.,* 2001)

Contd...

Table 2.1–*Contd...*

Activity	*Extract/Preparation*	*Organism/Model*	*Results*	*Reference*
DNA ladder formation stimulation	Infusion	Cell culture	Active	(Zhang *et al.,* 2000)
	Infusion	Cell culture	Weak activity	(Zhang *et al.,* 2000)
DNA synthesis inhibition	Hot H_2O extract	Cell culture	Active	(Melzig *et al.,* 2003)
DNA synthesis inhibition	Polyphenolic fraction	Cell culture	Active	(Klein *et al.,* 2002)
Endopeptidase stimulation	Hot H_2O extract	Cell culture	Active	(Melzig *et al.,* 2003)
Endothelin inhibition	Pigment	Rabbit	Active	(Xuan *et al.,* 2000)
Estradiol secretion stimulation	H_2O extract	Rat (Ovariectomized)	Active	(Das *et al.,* 2005)
Fibroblast growth factor release inhibition	Hot H_2O extract	Cell culture	Active	(Sartippour *et al.,* 2002)
Food-drug interaction	Hot H_2O extract	Human adult	Inactive	(Greenblatt *et al.,* 2006)
Free radical formation inhibition	Polyphenolic fraction	Cell culture	Active	(Steel *et al.,* 2000)
	Hot H_2O extract	Cell culture	Active	(Steel *et al.,* 2000)
Gastric emptying time decreased	Saponin fraction	Mouse	Active	(Murakami *et al.,* 2000)
Gastrointestinal disorders	H_2O extract	Human adult	Active	(Pisters *et al.,* 2001)
Glucuronyl transferase stimulation	Decoction	Rat male	Active	(Marnewick *et al.,* 2003)
Glucuronyl transferase stimulation	Hot H_2O extract	Rat female	Inactive	(Maliakal *et al.,* 2001)
Glutathione formation induction	Decoction	Rat male	Active	(Marnewick *et al.,* 2003)
Glutathione formation induction	Hot H_2O extract	Rat	Active	(Maity *et al.,* 2001)
Glutathione formation induction	Polyphenolic fraction	Cell culture	Active	(Steel *et al.,* 2000)
	Hot H_2O extract	Cell culture	Inactive	(Steel *et al.,* 2000)
Glutathione-*S*-transferase induction	Decoction	Rat male	Active	(Marnewick *et al.,* 2003)
Glutathione-*S*-transferase inhibition	Hot H_2O extract	Rat female	Active	(Maliakal *et al.,* 2001)
Hepatoprotective activity	Polyssacharide fraction	Female mice	Active	(Xu *et al.,* 2012)
	EtOH extract	Rat male	Active	(Schmitz *et al.,* 2009)

Contd...

Table 2.1–*Contd...*

Activity	*Extract/Preparation*	*Organism/Model*	*Results*	*Reference*
Histamine release inhibition	Polyphenolic fraction	Cell culture	Active	(Tachibana *et al.,* 2000)
Hydrogen peroxide release inhibition	EtOH (80 per cent) extract	Gerbil female	Active	(Hong *et al.,* 2001)
Hydroxyproline inhibition	H_2O extract	Rat (Ovariectomized)	Active	(Das *et al.,* 2005)
Hypocholesterolemic activity	H_2O extract	Human adult	Active	(Santana *et al.,* 2008)
	Powder	Rat male	Active (Liver)	(Hasegawa *et al.,* 2003)
	Powder	Rat male	Active (Plasma)	(Hasegawa *et al.,* 2003)
	H_2O extract	Human adult	Active	(Dulloo *et al.,* 2000)
Hypothermic activity	MeOH-H_2O(1:1) extract	Mouse	Active	(Chattopadhyay *et al.,* 2004)
I-Kappa-B Kinase inhibition	Polyphenolic fraction	Rat	Active	(Yang *et al.,* 2001)
Immunomodulatory activity	H_2O extract	Human adult	Active	(Levites *et al.,* 2002)
Inositol phosphate formation inhibition	Catechin fraction	–	Active	(Kang *et al.,* 2001)
Insulin potentieting effect	Leaves	–	Weak activity	(Broadhurst *et al.,* 2000)
Intestinal motility stimulation	Hot H_2O extract	Rat	Active	(Maity *et al.,* 2001)
	Saponin fraction	Mouse	Active	(Murakami *et al.,* 2000)
Iron absorption decreased	Infusion	Human adult	Active	(Samman *et al.,* 2001)
LDL oxidation inhibition	Infusion	–	Active	(Richelle *et al.,* 2001)
	Phenol-water extract	–	Active	(Mukoda *et al.,* 2001)
	$CHCl_3$ soluble fraction	Cell culture	Active	(Yang *et al.,* 2000)
	EtOAc soluble fraction	Cell culture	Active	(Yang *et al.,* 2000)
	H_2O soluble fraction	Cell culture	Inactive	(Yang *et al.,* 2000)
Lipid peroxide formation inhibition	Infusion	Rat male	Active	(Altiner *et al.,* 2000)
	Phenol-water extract	–	Active	(Mukoda *et al.,* 2001)
	EtOH (70 per cent) extract	Gerbil female	Active	(Hong *et al.,* 2001)

Contd...

Table 2.1–*Contd...*

Activity	*Extract/Preparation*	*Organism/Model*	*Results*	*Reference*
Locomotor activity decrease	EtOH (70 per cent) extract	Gerbil female	Active	(Hong *et al.,* 2001)
Luciferase stimulation	Phenolic fraction	Cell culture	Active	(Abou *et al.,* 2001)
Neuroprotective effect	Polyphenolic fraction	Cells PC-12	Active	(Levites *et al.,* 2002)
	Polyphenolic fraction	Neuroblasthoma human	Active	(Levites *et al.,* 2002)
NF Kappa-B binding inhibition	Polyphenolic fraction	–	Active	(Levites *et al.,* 2002)
Nitric oxide synthase stimulation	Hot H_2O extract	Rat	Active	(Maity *et al.,* 2001)
Nitric oxide synthesis inhibition	Infusion	Cell culture	Active	(Sarkar and Bhaduri 2001)
Ornithine descarboxylase inhibition	Hot H_2O extract	Cell culture	Active	(Steel *et al.,* 2000)
Phosphorylation inhibition	Polyphenolic fraction	Cell culture	Active	(Klein *et al.,* 2002)
Phototoxicity inhibition	Polyphenolic fraction	Active	Active	(Carini *et al.,* 2002)
Phytoestrogenic effects	Aqueous extract	Female rat	Active	(Das *et al.,* 2005)
Plaquet formation suppressant	Pigment	Rabbit	Active	(Xuan *et al.,* 2000)
Pletelet aggregation inhibition	Catechin fraction	–	Active	(Kang *et al.,* 2001)
Protein expression stimulation	Phenolic fraction	Cell culture	Active	(Abou *et al.,* 2001)
Protein photoaggregation inhibition	Infusion	Cell culture	Active	(Thiagarajan *et al.,* 2001)
Quinine reductase induction	Polyphenolic fraction	Cell culture	Inactive	(Steel *et al.,* 2000)
	Hot H_2O extract	Cell culture	Inactive	(Steel *et al.,* 2000)
Radical scavenging effect	Phenol-water extract	–	Active	(Mukoda *et al.,* 2001)
	EtOH-H_2O (50 per cent) extract	–	Active	(Chung *et al.,* 2001)
	Tannin fraction	Cell culture	Active	(Yokozawa *et al.,* 2000)
Radioprotective effect	Polyphenolic fraction	Human adult	Active	(Elmets *et al.,* 2001)
Renal function improvement	Polyphenolic fraction	Rabbit	Active	(Hu *et al.,* 2000)

Contd...

Table 2.1–*Contd...*

Activity	*Extract/Preparation*	*Organism/Model*	*Results*	*Reference*
Smooth muscle relaxant activity	H_2O extract	Species not stated	Active	(Hung *et al.,* 2002)
Superoxide dismutase stimulation	Infusion	Mouse male	Active	(Das *et al.,* 2002)
Superoxide production inhibition	Infusion	Cell culture	Active	(Sarkar *et al.,* 2001)
	Infusion	Cell culture	Active	(Thiagarajan *et al.,* 2001)
	Saponin fraction	–	Active	(Chaudhuri *et al.,* 2001)
Superoxide radical scavenging	Infusion	Cell culture	Active	(Thiagarajan *et al.,* 2001)
Superoxide scavenging activity increase	Phenol-water extract	–	Active	(Mukoda *et al.,* 2001)
Thermogenic activity	H_2O extract	–	Active	(Dulloo *et al.,* 2000)
α-Tocopherol depletion prevention	Infusion	Rat	Active	(Loes *et al.,* 2002)
Toxic effect (general)	Type extract not stated	Human adult	Inactive	(Maron *et al.,* 2003)
Tumor necrosing factor inhibition	Polyphenolic fraction	Mouse	Active	(Suganuma *et al.,* 2001)
Tumor promoting effect	Catechin fraction	Rat male	Inactive (Lung)	(Hirose *et al.,* 2001)
	Catechin fraction	Rat male	Inactive (Thyroid gland)	(Hirose *et al.,* 2001)
	Catechin fraction	Rat male	Inactive (Colon)	(Hirose *et al.,* 2001)
UDP-Glucuronyl transferase stimulation	Hot H_2O extract	Rat female	Active	(Maliakal *et al.,* 2001)
Urease inhibition	MeOH-H_2O extract	Gerbil male	Active	(Matsubara *et al.,* 2000)
Weight gain inhibition	H_2O extract	Rat	Active	(Dulloo *et al.,* 2000)
Weight loss	H_2O extract	Rat	Active	(Dulloo *et al.,* 2000)
	EtOH (80 per cent) extract	Human adult	Active	(Chantre and Lairon 2002)

Table 2.2: Presence of Compounds in *C. sinensis.*

Substances	*Compound Type*	*References*
Arachidic acid	Lipid	Akhlas *et al.,* 2000
Ascorbic acid	Vitamin	Hasegawa *et al.,* 2000
Assamsaponin C	Triterpene	Li *et al.,* 2013
Assamsaponin G	Triterpene	Murakami *et al.,* 2000
Assamsaponin I	Triterpene	Murakami *et al.,* 2000
Assamsaponin J	Triterpene	Murakami *et al.,* 2000
Astragalin	Flavonol	Luo 2012, Zhou and Peng 2000
Caffeine	Alkaloid	Horie *et al.,* 2002, Keya *et al.,* 2003, Koshiishi *et al.,* 2001, Robb *et al.,* 2002
Camelliquercetiside A	Flavonoid	Manir *et al.,* 2012
Camelliquercetiside B	Flavonoid	Manir *et al.,* 2012
Camelliquercetiside C	Flavonoid	Manir *et al.,* 2012
Camelliquercetiside D	Flavonoid	Manir *et al.,* 2012
(-)-Catechin-3-*O*-gallate	Flavonoid	Baumann *et al.,* 2001, Degenhardt, and Winterhalter 2000, Kang *et al.,* 2000, Leung *et al.,* 2001, Mauri and Pietta 2000
(+)-Catechin	Flavonoid	Luo *et al.,* 2012, Robb *et al.,* 2002, Zhou and Yang 2000
Chakasaponnin I	Saponin	Hamao *et al.,* 2011
Chakasaponnin II	Saponin	Hamao *et al.,* 2011
Chakasaponnin III	Saponin	Hamao *et al.,* 2011
Chlorogenic acid	Phenylpropanoid	Zhang *et al.,* 2001, Zhou *et al.,* 2000
Chrysanthemin	Flavonoid	Terahara *et al.,* 2001

Contd...

Table 2.2–*Contd...*

Substances	*Compound Type*	*References*
Coniferin	Phenylpropanoid	Zhou *et al.,* 2000
Delphinidin-3-*O*-β-*D*-(6-*trans*-*p*-coumaroyl)-galactopyranoside	Flavonoid	Terahara *et al.,* 2001
Delphinidin-3-*O*- β-*D*-glucoside	Flavonoid	Terahara *et al.,* 2001
Delphinidin-3-*O*- β-*D*-galactopyranoside	Flavonoid	Terahara *et al.,* 2001
Desacyl-floratheasaponin B	Saponin	Hamao *et al.,* 2011
Epiafzelechin-3-*O*-gallate	Flavonoid	Degenhardt *et al.,* 2000
(-)-Epiafzelechin-3-*O*-gallate	Flavonoid	Zhou *et al.,* 2000
(-)-Epicatechin	Flavonoid	Leung *et al.,* 2001, Luo *et al.,* 2012, *et al.,* Kang *et al.,* 2000, Robb *et al.,* 2002, Zhou *et al.,* 2000
(-)-Epigallocatechin	Flavonoid	Leung *et al.,* 2001, Luo *et al.,* 2012, Kang *et al.,* 2000, Mauri *et al.,* 2000, Robb *et al.,* 2002, Zhou *et al.,* 2000
(-)-Epigallocatechin-3-*O*-gallate	Flavonoid	(Baumann *et al.,* 2001, Degenhardt *et al.,* 2000, Leung *et al.,* 2001, Luo *et al.,* 2012, Kang *et al.,* 2000, Mauri *et al.,* 2000, Robb *et al.,* 2002, Zhou *et al.,* 2000, Umashankar *et al.,* 2001
Epitheaflavic acid	Flavonoid	Degenhardt *et al.,* 2001
Gallic acid	Benzenoid	Luo *et al.,* 2012, Zhou *et al.,* 2000
(+)-Gallocatechin	Flavonoid	Luo *et al.,* 2012, Robb *et al.,* 2002
4-Hydroxy-benzoic acid	Benzenoid	Pietta *et al.,* 2000
4-Hydroxy-3-methoxy-hippuric acid	Proteid	Pietta *et al.,* 2000
3-(4-Hydroxy-phenyl)-propionic acid	Phenylpropanoid	Pietta *et al.,* 2000
Isoquercetin	Flavonol	Zhou *et al.,* 2000
Isoschaftoside	Flavone	Wada *et al.,* 2000
Isotheasaponins B1	Saponin	Kobayashi *et al.,* 2006

Contd...

Table 2.2–*Contd...*

Substances	*Compound Type*	*References*
Isotheasaponins B2	Saponin	Kobayashi *et al.,* 2006
Isotheasaponins B3	Saponin	Kobayashi *et al.,* 2006
Isovitexin	Flavonoid	Luo *et al.,* 2012
Kaempferol	Flavonol	Zhou *et al.,* 2000
Kaempferol-3-*O*-[α-l-rhamnopyranosyl(1-3)-α-l-rhamnopyranosyl (1-6)-β-*D*-galactopyranoside]	Flavonol	Lakenbrink *et al.,* 2000
Kaempferol-3-*O*-[α-l-rhamnopyranosyl(1-3)-α-l-rhamnopyranosyl (1-6)-β-*D*-glucopyranoside]	Flavonol	Lakenbrink *et al.,* 2000
Kaempferol-3-*O*-[α-l-rhamnopyranosyl(1-3)-(4'''-*O*-acetyl)-α-l-rhamnopyranosyl(1-6)-β-*D*-glucopyranoside]	Flavonol	Lakenbrink *et al.,* 2000)
Kaempferol-3-*O*-[β-*D*-glucopyranosyl(1-3)-α-l-rhamnopyranosyl (1-6)-β-*D*-galactopyranoside]	Flavonol	Wada *et al.,* 2000
Kaempferol-3-*O*-[β-*D*-glucopyranosyl(1-3)-α-l-rhamnopyranosyl(1-6)-β-*D*-glucopyranoside]	Flavonol	Wada *et al.,* 2000
α-Linolenic acid	Lipid	Luo *et al.,* 2012
Linoneic acid	Lipid	Akhlas *et al.,* 2000
4-Methyl-catechol	Benzenoid	Pietta *et al.,* 2000
Myristic acid	Lipid	Akhlas *et al.,* 2000
Nicotiflorin	Flavonol	Degenhardt *et al.,* 2000, Zhou *et al.,* 2000
Oleic acid	Lipid	Akhlas *et al.,* 2000
3*R*,9*R*-Oxide-5-megastigmene	Isoprenoid	Luo *et al.,* 2012
Palmitic acid	Lipid	Akhlas *et al.,* 2000
Protocatechuic acid	Benzenoid	Pietta *et al.,* 2000
Quercetin	Flavonol	Zhou *et al.,* 2000

Contd...

Table 2.2–*Contd...*

Substances	*Compound Type*	*References*
Quercetin-3-*O*-[β-*D*-glucopyranosyl(1-3)-α-l-rhamopyranosyl (1-6)-β-*D*-galactopyranosyde]	Flavonol	Wada *et al.,* 2000
Quercetinn-3-*O*-[β-*D*-glucopyranosyl(1-3)-α-l-rhamopyranosyl (1-6)-β-*D*-glucopyrannoside]	Flavonol	Wada *et al.,* 2000
Rutin	Flavonol	Degenhardt *et al.,* 2000, Zhou *et al.,* 2000
Stearic acid	Lipid	Akhlas *et al.,* 2000
Strictin	Tannin	Luo *et al.,* 2012
Strictinin	Tannin	Degenhardt *et al.,* 2000, Zhou *et al.,* 2000
Theaflavin	Flavonoid	Catterall *et al.,* 2003
Theaflavin 1	Flavonoid	Leung *et al.,* 2001
Theaflavin-3'-gallate B	Flavonoid	Leung *et al.,* 2001
Theaflavin-3-3'-digallate	Flavonoid	Leung *et al.,* 2001
Theaflavin-3-gallate A	Flavonoid	Leung *et al.,* 2001
Theanine	Proteid	Xu *et al.,* 2002, Zhou *et al.,* 2002
Thenaphthoquinone	Flavonoid	Tanaka *et al.,* 2000
Theobromine	Alkaloid	Robb *et al.,* 2002
Theogallin	Benzenoid	Zhou *et al.,* 2000
Theanine	Proteid	He *et al.,* 2000
Theasaponin A-8	Triterpene	Li *et al.,* 2013
Theasaponin A-9	Triterpene	Li *et al.,* 2013
Theasaponin C-1	Triterpene	Li *et al.,* 2013
Theasaponin E-1	Triterpene	Li *et al.,* 2013

Contd...

Table 2.2–*Contd...*

Substances	*Compound Type*	*References*
Theasaponin E-2	Triterpene	Li *et al.,* 2013, Murakami *et al.,* 2000, Tomita *et al.,* 2000
Theasaponin H-1	Triterpene	Li *et al.,* 2013
TR-saponin A	Triterpene	Lu *et al.,* 2000
TR-saponin B	Triterpene	Lu *et al.,* 2000
TR-saponin C	Triterpene	Lu *et al.,* 2000
Vanillic acid	Benzenoid	Pietta *et al.,* 2000

compilations copied from other sources. For details, the original references should be consulted.

Nutraceutical Aspects

Anti-diabetic Activity

The study conducted by Islam *et al.* (2011) investigated the effects of a 0.5 per cent aqueous extract of white tea in a streptozotocin-induced diabetes model of rats. Six-week-old male Sprague-Dawley rats were divided into 3 groups of 6 animals in each group namely: normal control (NC), diabetic control (DBC) and diabetic white tea (DWT). Diabetes was induced by an intraperitoneal injection of streptozotocin (65 mg/kg BW) in DBC and DWT groups except the NC group. After 4 weeks feeding of 0.5 per cent aqueous extracts of WT, the drink intake was significantly ($p < 0.05$) increased in the DWT group compared to the DBC and NC groups. Blood glucose concentrations were significantly decreased and glucose tolerance ability was significantly improved in the DWT group compared to the DBC group. Liver weight and liver glycogen were significantly increased and serum total cholesterol and LDL-cholesterol were significantly decreased in the DWT group compared to the DBC group. The food intake, body weight gain, serum insulin and fructosamine concentrations were not influenced by the consumption of white tea (WT). Data of this study suggest that the 0.5 per cent aqueous extract of WT is effective to reduce most of the diabetes-associated abnormalities in a streptozotocin-induced diabetic model of rats.

In another study, Sabu *et al.* (2002) investigated the effect of crude polyphenolic fraction of green tea in reducing the alloxan-induced oxidative damage and diabetes in rats. An aqueous solution of green tea polyphenols (GTP) was found to inhibit lipid peroxidation (LP), scavenge hydroxyl and superoxide radicals *in vitro*. Concentration needed for 50 per cent inhibition of superoxide, hydroxyl and LP radicals were 10, 52.5 and 136 mg/ml, respectively. Administration of GTP (500 mg/kg b.wt.) to normal rats increased glucose tolerance significantly (PB/0.005) at 60 min. GTP was also found to reduce serum glucose level in alloxan diabetic rats significantly at a dose level of 100 mg/kg b.wt. continued daily administration (15 days) of the extract 50, 100 mg/kg b.wt. exhibiting 29 and 44 per cent reduction in the elevated serum glucose level produced by alloxan administration. Elevated hepatic and renal enzymes produced by alloxan were found to be reduced (PB/0.001) by GTP. The serum LP levels which was increased by alloxan and was reduced significantly (PB/0.001) by the administration of 100 mg/kg b.wt. of GTP. Decreased liver glycogen, after alloxan administration, showed a significant (PB/0.001) increase after GTP treatment. GTP treated group showed increased antioxidant potential as seen from improvements in superoxide dismutase and glutathione levels. However, catalase, LP and glutathione peroxidase levels were unchanged. Those results indicate that alterations in the glucose usage system and oxidation status in rats increased by alloxan were partially reversed by the administration of the glutamate pyruvate transaminase.

Anti-obesity Effects

The methanolic extract from the flower buds of *C. sinensis* cultivated in Fujian Province showed inhibitory effects on body weight gain and the weight of visceral fats in high-fat diet-fed mice and/or Tsumura Suzuki Obese Diabetic (TSOD) mice. A suppressive effect of the extract on food intake was suggested to contribute to the anti-obesity effect. The *n*-butanol (BuOH)-soluble fraction also reduced food intake in normal diet-fed mice. A principal constituent, chakasaponin II, inhibited gastric emptying (GE) as well as food intake. These inhibitory effects were partly reduced by the pre-treatment with a high dose of capsaicin. The *n*-BuOH-soluble fraction and chakasaponin II suppressed mRNA levels of neuropeptide Y (NPY), an important regulator of body weight through its effects on food intake and energy expenditure, in the hypothalamus. Furthermore, chakasaponin II enhanced the release of serotonin (5-HT) from the isolated ilea of mice *in vitro*. These findings suggested that the active saponins suppressed the appetite signals in the hypothalamus through stimulation of the capsaicin-sensitive sensory nerves, probably vagal afferent nerves, or enhancement of 5-HT release from the ilea, leading to reduced food intake and body weight gain (Hamao *et al.,* 2011).

Anti-inflammatory, Analgesic and Antipyretic Activity

Nutraceutical studies were carried out with methanol-water (1:1) extract of dried tea (*C. sinensis*) root extract (TRE). TRE was found to possess anti-inflammatory, analgesic and antipyretic activities at $1/10^{th}$ of its LD_{50} dose of 100 mg/kg i.p. It was found that TRE inhibited the arachidonic acid-induced paw edema in rats which indicated that TRE produced the anti-inflammatory activity by inhibiting both the cyclooxygenase and lypooxygenase pathways of arachidonic acid metabolism. TRE also enhanced peritoneal cell count and the number of macrophages in normal mice. It is plausible that the saponins present in TRE may be responsible for these activities of TRE (Chattopadhyay *et al.,* 2004). Earlier studies have reported that tea root extract (TRE) possesses antitumor effect in ascites (Sur, 1994). Preliminary studies have also revealed the anti-inflammatory and antioxidant properties of the saponins isolated from TRE (Lu *et al.,* 2000).

Chemopreventive Effects

Based on studies with green and black teas, polyphenolic components have been considered as potential chemopreventive agents. Tea polyphenols are known to modulate the metabolic fate of carcinogens in several ways to render them less active, thus protecting the target tissue against their adverse effects. Several studies in animals showed that black and green teas modulate cancer development *in vivo*. The consumption of tea polyphenols and tea pigments, comprising the oxidized flavanol products, theaflavins and thearubigins, significantly reduced the number as well as the average area of glutathione-*S*-transferase placental form positive ($GSTP^+$) foci in the liver. An aqueous extract of green tea inhibited both cancer initiation and promotion of AFB1- and carbon tetrachloride-induced hepatocarcinogenesis in male Fischer rats (Marnewick *et al.,* 2009).

Cytotoxic and Apoptogenic Effects

The polyphenolic compounds present in green tea showed cancer chemopreventive effect both *in vivo* and *in vitro*. Since it was found that tea root extract (TRE) inhibited Ehrlich ascites carcinoma (EAC) in mice, the methanol-water extract of tea root was investigated, and two of its saponins isolated from the butanolic fraction of the root extract for their anticancer effect on K562, an erythroleukemic cell line and on U937, a human leukemic cell line and also on cells of untreated patients with either chronic myeloid leukemia (CML) or acute lymphoid leukemia (ALL). The anticancer activity of di- and tri-terpenes and other polyphenolic compounds present in tea is already reported. The cytotoxic and apoptogenic effect of tea root extract were evaluated (TRE), and two of its steroidal saponins named as TS1 and TS2, on human cell lines and on cells from leukemic patients. It was found that TRE, TS1 and TS2 significantly decreased cell count and that TRE caused apoptosis, as confirmed morphologically by confocal microscopy and by flow-cytometric analysis using Annexin-V fluorescein isothiocyanate (FITC) and propidium iodide (PI). Cell count and MTT assay in normal white blood cells (WBC) of healthy volunteers revealed that TRE produced insignificant reduction in cell count and cytotoxicity (Ghosh *et al.*, 2006).

Hepatoprotective Activity

Schmitz *et al.* (2009) evaluated the hepatic protection effect of the green tea extract (GTE) on lipoperoxidation and necrosis, induced by the carcinogenic diethylnitrosamine (DEN) in rat's liver. Adult male Wistar rats were used and exposed to one only intra peritoneal dose of 200 mg/kg of DEN, and orally 120 mg/kg of GTE in different experimental moments. After 24 h of a DEN treatment, the animals were sacrificed and the following aspects were evaluated: the AST/ALT levels in plasma, lipoperoxidation of TBARS and FOX in the liver. Necrosis and hepatic hemorrhage were observed through a histological examination. The chemoprotector action and the decrease in lipoperoxidation were detected after a decrease of AST/ALT, TBARS, FOX and hepatic necrosis. The evaluation of these results confirmed the importance of the use of the green tea as a chemoprotector agent, particularly as a preventive method.

Toxicity Studies

In study realized by Hsu *et al.* (2011), mice were orally administered (gavage) with green tea extract at doses of 0 (as normal group), 625, 1250 and 2500 mg/kg body weight/day for 28 days. The results showed that oral administration of green tea extract did not cause adverse effects on body weight, organ weights, hematology, serum biochemistry, urinalysis or histopathology. Additionally, administering green tea extract via gavage significantly reduced triglyceride and cholesterol levels. These observed effects could be attributed to the high levels of catechins present in green tea as these compounds have been reported to have beneficial health effects. The non-observed adverse effect level for green tea extract derived from the results of the present study was 2500 mg/kg body weight/day. The results of the present study clearly showed that oral administration of green tea extract at up to 2500 mg/kg body

weight/day for 28 days did not cause either mortality or toxicity mice, regardless of gender.

Additionally, *in vitro* studies reported that administration of rat hepatocytes with high concentrations of EGCG resulted in reduced cell viability (Galati *et al.,* 2006). *In vivo* studies also suggest that administration with a single dose of 1500 mg/kg, i.g. EGCG in mice may result in hepatotoxicity (Lambert *et al.,* 2010). Due to numerous interactions and synergisms, it is difficult to study the effects of natural dietary supplements on human health when administered in complex mixtures as opposed to a purified compound (Vitaglione *et al.,* 2004). Thus, a conscientious and careful safety evaluation of green tea extract is necessary.

Clinical Efficacy

Previous study demonstrated that the association between soy and green tea diminishes hypercholesterolemia and increases total plasma antioxidant potential in dyslipidemic subjects. No significant difference occurred in low density lipoprotein (LDL), high-density lipoprotein (HDL) cholesterol, and triacylglycerol levels across groups. However, a statistically significant difference in total cholesterol occurred within the soy/green tea group 45 and 90 d after intervention. No statistically significant difference occurred in plasma levels of lipid hydroperoxides or those linked to LDL in any of the groups studied. All the groups that used soy and/or green tea presented increased total plasma antioxidant potential. Soy and green tea, alone or in combination, increased the total antioxidant potential of hypercholesterolemic patients, whereas only the combination decreased total cholesterol levels (Santana *et al.,* 2008).

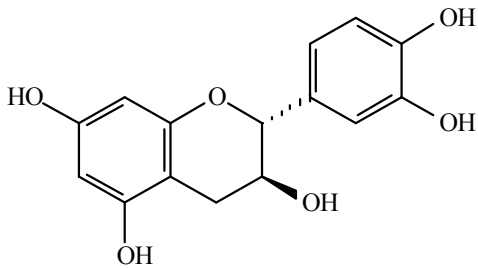
Chemical Constituents

There are numerous studies about the composition of *C. sinensis* demonstrating that teas contain purine alkaloids (xanthines), phenolic compounds (catechins, *O*-glycosylated flavonols, *C*-glycosylated flavones, proanthocyanidins and phenolic acids and their derivatives), terpenoids, fatty acids, essential oils and amino acids. Oolong and black teas also contain the oxidation products of catechins, theaflavins and polymeric thearubigins (Scoparo *et al.,* 2012). Flavan-3-ols (catechins), which are abundant in young leaves and shoots of the tea plant, account for approximately 70-80 per cent of tea polyphenols.

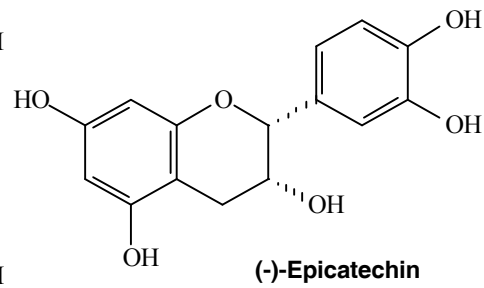
Camellia sinensis contains high levels of polyphenols, including (+)-catechin, (-)-epicatechin, (-)-catechin gallate, (-)-epicatechin gallate, (-)-epigallocatechin, (+) gallocatechin, (-)-epigallocatechin gallate, (-)-gallocatechin gallate (Figure 2.3). Content of catechins varies with climate, season, horticultural practices, leaf age and variety. Polyphenols from *C. sinensis* are efficient free radical and singlet oxygen scavengers (Balentine *et al*., 1997).

Other important groups of polyphenols in tea are flavonols; water-soluble compounds make up to 3 per cent of dry weight of tea leaves. Main flavonols are myricetin, quercetin and kaempferol. They are present in plants as glycosides and aglycones. Sugar moieties consist of glucose, rhamnose, galactose, arabinose and fructose (Balentine *et al*., 1997). Tea flavonoid consumption has been linked to lower

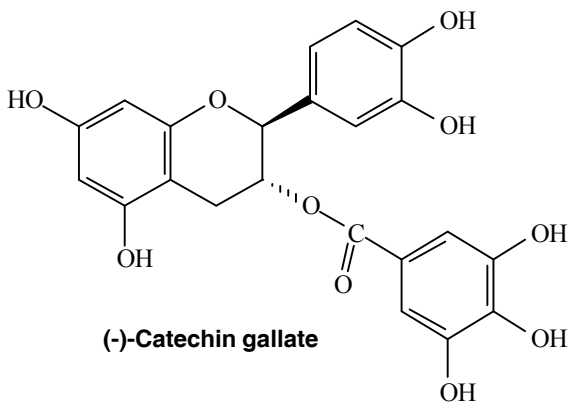
Figure 2.3: Chemical Structures of some Chemical Constituents of *C. sinensis*.



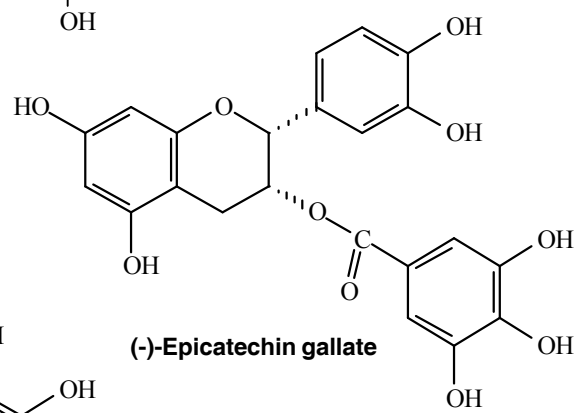
(+)-Catechin



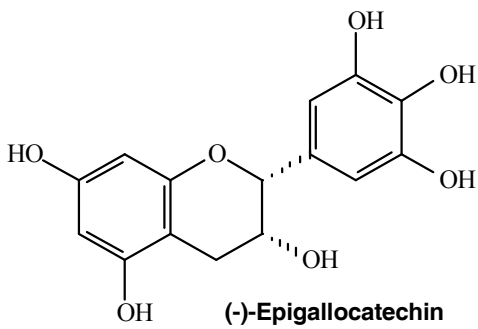
(-)-Epicatechin



(-)-Catechin gallate



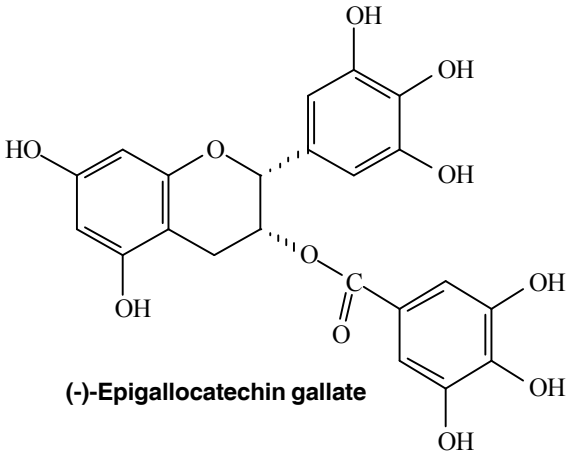
(-)-Epicatechin gallate



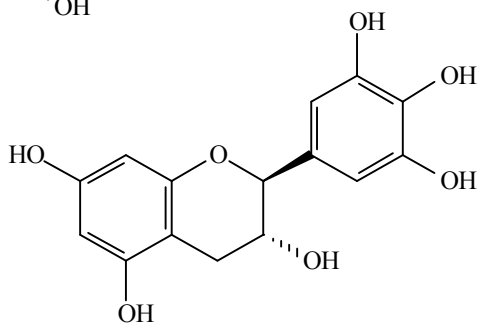
(-)-Epigallocatechin

Contd...

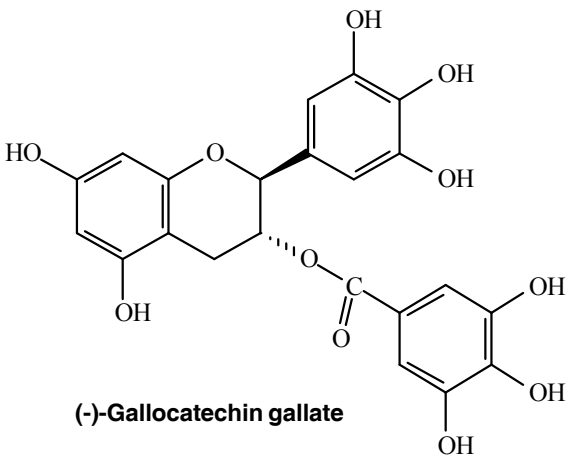
Figure 2.3–*Contd...*



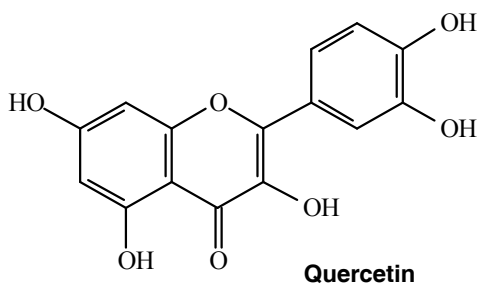
(-)-Epigallocatechin gallate



(+)-Gallocatechin



(-)-Gallocatechin gallate



Quercetin

incidences of chronic diseases such as cardiovascular disease and cancer. It has been shown, in different cell lines and animal models, that tea flavonoids inhibit cell proliferation, induce cell cycle arrest and apoptosis, stimulate angiogenesis and affect cell signaling pathways. The health benefits associated with tea consumption have been attributed in part to the antioxidant and free radical-scavenging activity of the most abundant tea flavonols (Rusak *et al.*, 2008).

Bioactivity of Metabolites

Study conducted by Li *et al.* (2013) described the bioactivity-guided fractionation of the crude ethanol extract of seeds of *C. sinensis*, leading to the isolation of seven theasaponins: theasaponin E1, theasaponin E2, theasaponin C1, assamsaponin C, theasaponin H1, theasaponin A9, and theasaponin A8. The fraction of total tea seed saponin showed anti-tumor activity in S180 implanted ICR mice and the isolated theasaponins exhibited different tumor inhibitory effects against human tumor cell lines, respectively. At the same time, the quinone reductase inducing activities were also estimated to reveal the possibility of tea seed for use as a chemopreventive agent of tumor. The tea seed triterpene saponin (TS) from *Camellia sinensis* was found to exhibit better antitumor activity *in vivo* in S180 implanted ICR mice and QR inducing activity for hepa lclc7 cells respectively compared with the total tea seed saponin (TTS), hydrolysate of the TTS and tea seed flavonoid glycosides (TF). By bioassay-guided isolation, the TS fraction was separated and seven major components were purified and identified as theasaponin E1, theasaponin E2, theasaponin C1, assamsaponin C, theasaponin H1, theasaponin A9, and theasaponin A8.

Several epidemiologic studies have proposed an association between green tea consumption and a reduced risk of different kinds of human cancer. For instance, it has been suggested that epigallocatechin gallate (EGCG), a major polyphenolic antioxidant present in green tea, may protect cells against cancer initiation and subsequent progression by its antioxidant activity (Kativar *et al*., 1997). In particular, EGCG has been the focus of research in recent years due to its relatively high levels in green tea and higher antioxidant activity. Indeed, a considerable body of literature has shown that EGCG arrests the progression of hepatic fibrosis and prevents carbon tetrachloride (CCl_4)-induced liver injury in animal models by inhibiting oxidative damage. EGCG has also been shown to inhibit lipopolysaccharide-induced tumor necrosis factor-α and inducible nitric oxide synthase production in mice. Although EGCG is the most plentiful of the green tea catechins and exhibits a high level of antioxidant activity, preventive effects appear to be stronger when a mixture of tea catechins, such as polyphenon E, a decaffeinated green tea catechin mixture, or a green tea extract, is administered (Hsu *et al.*, 2011).

The results of many investigations showed potential antioxidant proprieties of tea polyphenols. The tea catechins can act as antioxidants by donation of hydrogen atom, as an acceptor of free radicals, interrupter of chain oxidation reactions or by chelating metals (Gramza and Korczak, 2004).

Conclusion

The consumption of different types of tea derived from *Camellia sinensis* is most often associated to their antioxidant properties. An increasing number of scientific

researches are performed in an attempt to better understand the mechanisms of action of antioxidants, the benefits associated with the antioxidant capacity and the best way to optimize such properties. Investigations related to the ideal consumption of green tea suggest that it may have a beneficial effect on human health. However, more research is needed to elucidate the properties and mechanisms of action of phenolic compounds in this drink enjoyed worldwide.

Acknowledgements

The authors wish to express their sincere thanks to the College of Pharmacy, The University of Illinois at Chicago, Chicago, Illinois 60612-7231, U.S.A., for helping with the computer aided NAPRALERT search and Brazilian agencies CNPq and FACEPE for financial support.

Abbreviations

ALL:	Acute Lymphoid Leukemia
ALT:	Alanine aminotranferease
AST:	Aspartate aminotransferase
CHD:	Chronic Heart Disease
CML:	Chronic Myeloid Leukemia
CVD:	Cardio Vascular Diseases
DBC:	Diabetic control
DEN:	Diethylnitrosamine
DHA:	Docosahexaenoic acid
DWT:	Diabetic White Tea
EAC:	Ehrlich Ascites Carcinoma
EGC:	(-)-epigallocatechin
EGCG:	(-)-epigallocatechin-3-gallate
FITC:	Fluorescein isothiocyanate
FOX:	Ferrous oxidation in xylenol orange
GE:	Gastric Emptying
GI:	Glycemic Index
GSTP:	Glutathione-*S*-transferase placental
GTE:	Green Tea Extract
GTP:	Green Tea Polyphenols
HDL-C:	High Density Lipoprotein-Cholesterol
LDL-C:	Low Density Lipoprotein-Cholesterol
LP:	Lipid peroxidation
MTT:	(3-[4,5-dimethylthiazol-2-yl]-2,5 diphenyl tetrazolium bromide)
NAPRALERT:	NAtural PRoducts ALERT
NC:	Normal control

NPY: Neuropeptide Y
PI: Propidium iodide
TBARS: Thiobarbituric Acid Reactive Substances
TRE: Tea (*C. sinensis*) Root Extract
TS: Triterpene saponin
TSOD: Tsumura Suzuki Obese Diabetic
TTS: Total Tea Seed Saponin
WBC: White Blood Cells
WT: White Tea

References

Abeywickrama, K.R.W., Ratnasooriya, W.D., and Amarakoon, A.M.T. (2011). Oral hypoglycaemic, antihyperglycaemic and antidiabetic activities of Sri Lankan Broken Orange Pekoe Fannings (BOPF) grade black tea (*Camellia sinensis* L.) in rats. *Journal of Ethnopharmacology*, **135**: 278-286.

Abou-Agag, L.H., Aikens, M.L., Tabengwa, E.M., Benza, R.L., Shows, S.R., Grenett, H.E., and Booyse, F.M. (2001). Polyphenolics increase t-pa and u-pa gene transcription in cultured human endothelial cells. *Alcoholism, Clinical and Experimental Research*, **25**: 155-162.

Adiwinata, H.O., Martosupono, M., and Schoorel, A.F. (1989). *Camellia sinensis*. In: Westphal, E and Jansen, PCM, PROSEA plant resources of Southeast Asia: a selection, 72-79.

Akhlas, M., Hussain, M., and Lodhi, K.A. (2000). Phytochemical studies of *Camellia sinensis* (L.) O. *Kuntze Hamdard Medicine*, **43**: 46-60.

Alessio, H.M., Hagerman, A.E., Romanello, M., Carando, S., Threlkeld, M.S, Rogers, J., Dimitrova, Y., Muhammed, S., and Wiley, R.L. (2002). Consumption of green tea protects rats from exercise induced oxidative stress in kidney and liver. *Nutrition Research*, **22**: 1177-1188.

Altiner, D.S., and Yenice, B. (2000). Effect of black tea on lipid peroxidation in carbon tetrachloride treated male rats. *Drug Metabolism and Drug Interaction*, **16**: 123-129.

Balentine, D.A., Wiseman, S.A., and Bouwens, L.C.M. (1997). The chemistry of tea flavonoids. *Critical Reviews in Food Science and Nutrition*, **37**: 693-704.

Baumann, D., Adler, S., and Hamburger, M. (2001). A simple isolation method for the major catechins in green tea using high-speed countercurrent chromatography. *Journal of Natural Products*, **64**: 353-355.

Bedoya, L.M., Palomino, S.S., Abad, M.J., Bermejo, P., and Alcami, J. (2002). Screening of selected plant extracts for *in vitro* inhibitory activity on human immunodeficiency virus. *Phytotherapy Research*, **16**: 550-554.

Besra, S.E., Gomes, A., Ganguly, D.K., and Vedasiromoni, Jr. (2003). Antidiarrhoeal activity of hot water extract of black tea (*Camellia sinensis*). *Phytotherapy Reseasrch*, **17**: 380-384.

Bhattacharyya, A., Choudhuri, T., Pal, S., Chattopadhyay, S. K., Datta, G., Sa, G., and Das, T. (2003). Apoptogenic effects of black tea on Ehrlich's ascites carcinoma cell. *Carcinogenesis*, **24**: 75-80.

Blot, W.J., Mc Laughlin, J.K., and Chow, W.H. (1997). Cancer rates among drinkers of black tea. *Food Science and Nutrition,* **37**: 739-760.

Broadhurst, C.L., Polansky, M.M., and Anderson, R.A. (2000). Insulin-like biological activity of culinary and medicinal plants aqueous extracts *in vitro*. *Journal of Agricultural and Food Chemistry*, **48**: 849-852.

Cabrera, C., Artacho, R., and Gimenez, R. (2006). Beneficial effects of green tea: a review. *Journal of the American College of Nutrition*, **25**: 79-89.

Carini, M., Aldini, G., Orioli, M., and Facino, R.M. (2002). Antioxidant and photoprotective activity of a lipophilic extract containing neolignans from *Krameria triandra* roots. *Planta Medica*, **63**: 193-197.

Catterall, F., McArdle, N.J., Mitchell, L., Papayanni, A., Clifford, M.N., and Ioannides, C. (2003). Hepatic and intestinal cytochrome P450 and conjugase activities in rats treated with black tea theafulvins and theaflavins. *Food and Chemical Toxicology,* **41**: 1141-1147.

Chan, E.W.C., Lim, Y.Y., and Chew, Y.L. (2007). Antioxidant activity of *Camellia sinensis* leaves and tea from a lowland plantation in Malaysia. *Food Chemistry*, **102**: 1214-1222.

Chantre, P., and Lairon, D. (2002). Recent findings of green tea extract Ar25 (Exolise) and its activity for the treatment of obesity. *Phytomedicine*, **9**: 3-8.

Chattopadhyay, P., Besra, S.E., Gomes, A., Das, M., Sur, P., Mitra, S., and Vedasiromoni, J.R. (2004). Anti-inflammatory activity of tea (*Camellia sinensis*) root extract. *Life Sciences*, **74**: 1839-1849.

Chaudhuri, P.S.T., Vedasiromoni, J.R., Gomes, A., and Ganguly, D.K. (2001). Anti-inflammatory and antioxidant property of saponins of tea [*Camellia sinensis* (L) O. Kuntze] root extract. *Phytotherapy Research*, **15**: 174-176.

Chauhan, D.S., Bhattacharya, S., and Ahmed, K.K.M. (2012). Comparative *in vitro* antioxidant evaluation of different extracts of *Camellia sinensis* leaves form different geographical locations in India. *Pharmacognosy Journal*, **33**: 46-49.

Chauhan, D.S., Bhattacharya, S., and Ahmed, K.K.M. (2013). Comparative *in vitro* antibacterial evaluation of different extracts of *Camellia sinensis* leaves form different geographical locations in India. *Pharmacognosy Journal*, **5**: 879-880.

Chung, J.S., Lee, M.S., and Chung, J.Y. (2001). Antioxidative activity of the extracts from the leaves and fruits of *Acer ginnala*. *Natural Product Sciences*, **7**: 45-48.

Chung, L.Y., Cheung, T.C., Kong, S.K., Fung, K.P., Choy, Y.M., Chan, Z.Y., and Kwok, T.T. (2001). Induction of apoptosis by green tea catechins in human prostate cancer DU 145 cells. *Life Sciences*, **68**: 1207-1214.

Costa, R.M., Magalhães, A.S., Pereira, J.A., Andrade, P.B. Valentão, P., Carvalho, M., and Silva, B.M. (2009). Evaluation of free radical-scavenging and antihemolytic activities of quince (*Cydonia oblonga*) leaf: A comparative study with green tea (*Camellia sinensis*). *Food and Chemical Toxicology*, **47**: 860-865.

Das, A.S., Das, D., Mukherjee, M., Mukherjee, S., and Mitra, C. (2005). Phytoestrogenic effects of black tea extract (*Camellia sinensis*) in an oophorectomized rat (*Rattus norvegicus*) model of osteoporosis. *Life Sciences,* **77**: 3049-3057.

Das, M., Sur, P., Gomes, A., Vedasiromoni, J.R., and Ganguly, D.K. (2002). Inhibition of tumor growth and inflammation by consumption of tea. *Phytotherapy Research*, **16(S1)**: S40-S44.

Degenhardt, A., and Winterhalter, P. (2001). Isolation of natural pigments by high speed CCC. *Journal of Liquid Chromatography and Related Technologies*, **24**: 1745-1764.

Degenhardt, A., Engelhardt, U.H., Lakenbrink, C., and Winterhalter, P. (2000). Preparative separation of polyphenols from tea by high-speed counter current chromatography. *Journal of Agricultural and Food Chemistry*, **48**: , 3425-3430.

Donovan, J.L., Chavin, K.D., Devane, C.L., Taylor, R.M., Wang, J.S., Ruan, Y., and Markowitz, J.S. (2008). Green tea (*Camellia sinensis*) extract does not alter cytochrome P450 3a4 or 2d6 activity in healthy volunteers. *Drug Metabolism and Disposition*, **32**: 906-908.

Dou, R.L., Liu S.D., Hu R.M., Sun, Z., Yang, H., and Shen, W. (2000). The protective effect of polyphenol on hepatic peroxidative damage in obstructive jaundice. *Acta Nutrimenta Sinica*, **22**: 328-332.

Duffy, S.J., Keaney, J.F. Jr., Holbrook, M., Gokce, N., Swerdloff, P.L., Frei, B., and Vita, J.A. (2001). Short- and long-term black tea consumption reverses endothelial dysfunction in patients with coronary artery disease. *Circulation,* **104**: 151-156.

Dulloo, A.G. (2000). Modulation of obesity of a green tea catechin. *American Journal of Clinical Nutrition,* **72**: 1232-1234.

Elmets, C.A., Singh, D., Tubesing, K., Matsui, M., Katiyar, S., and Mukhtar, H. (2001). Cutaneous photoprotection from ultraviolet injury by green tea polyphenols. *Journal of the American Academy of Dermatology,* **44**: 425-432.

Fadhel, Z.A., and Amran, S. (2002). Effects of black tea extract on carbon tetrachloride-induced lipid peroxidation in liver, kidneys, and testes of rats. *Phytotherapy Research*, **16(S1)**: S28-S32.

Frank, J., George, T.W., Lodge, J.K., Rodriguez-Mateos, A.M., Spencer, J.P.E., Minihane, A.M., and Rimbach, G. (2009). Daily consumption of an aqueous green tea extract supplement does not impair liver function or alter cardiovascular disease risk biomarkers in healthy men. *Jounal of Nutrition*, **139**: 58-63.

Galati, G., Lin, A., Sultan, A.M., and O'Brien, P.J. (2006). Cellular and *in vivo* hepatotoxicity caused by green tea phenolic acids and catechins. *Free Radical Biololgy and Medicine*, **40**: 570-580.

Ghosh, P., Besra, S.E., Tripathi, G., Mitra, S., and Vedasiromoni, J.R. (2006). Cytotoxic and apoptogenic effect of tea (*Camellia sinensis* var. *assamica*) root extract (TRE) and two of its steroidal saponins TS1 and TS2 on human leukemic cell lines K562 and U937 and on cells of CML and ALL patients. *Leukemia Research*, **30**: 459-468.

Gong, Y.Y., Han, C., and Chen, J.S. (2000). Effect of tea polyphenols and tea pigments on the inhibition of precancerous liver lesions in rats. *Nutrition and Cancer*, **38**: 81-86.

Graham, H.N. (1992). Green tea composition, consumption, and polyphenol chemistry. *Preventive Medicine*, **21**: 334-350.

Graham, H.N. (1999). Tea. In: Frederick. JF (Ed) *Wiley Encyclopedia of Food Science and Technology*, 2292-2305.

Gramza, A., and Korczak, J. (2004). Tea extracts influence on catalytical properties of Fe2C in lipids. *Polish Journal of Environmental Studies*, **13**: 143-146.

Greenblatt, D.J., von Moltke, L.L., Perloff, E.S., Luo, Y., Harmatz, J.S., and Zinny, M.A. (2006). Interaction of flurbiprofen with cranberry juice, grape juice, tea, and fluconazole: *in vitro* and clinical studies. *Clinical Pharmacology and Therapeutics*, **79**: 125-133.

Gupta, S., Hastak, K., Ahmad N., Lewin, J.S., and Mukhtar, H. (2001). Inhibition of prostate carcinogenesis in tramp mice by oral infusion of green tea polyphenols. *Proceeding of the National Academy of Sciences*, **98**: 10350-10355.

Hamao, M., Matsuda, H., Nakashima, S., Semura, S., Maekubo, S., Wakasugi, S., and Yoshikawa, M. (2011). Anti-obesity effects of the methanolic extract and chakasaponins from the flower buds of *Camellia sinensis* in mice. *Bioorganic and Medicinal Chemistry*, **19**: 6033-6041.

Hamilton-Miller, J.M.T. (2001). Anti-cariogenic properties of tea (*Camellia sinensis*). *Journal of Medical Microbiology*, **50**: 299-302.

Hasegawa, N., Niimi, N., and Odani, F. (2002). Vitamin C is one of the lipolytic substances in green tea. *Phytotherapy Research*, **16(S1)**: S91-S92.

Hasegawa, N., Yamda, N., and Mori, M. (2003). Powdered green tea has antilipogenic effect on zucker rats fed a high-fat diet. *Phytotherapy Research*, **17**: 477-480.

He, P., Wada, S., Watanabe, N., and Sugiyama, K. (2000). Liver injury-preventive effect of tea theanine in rats. *Journal of Food Science*, **65**: 30-33.

Hebert, J.L., Khugyani, F., Athar, M., Kopelovich, L., Epstein, E.H.Jr., and Aszterbaum, M. (2001). Chemoprevention of basal cell carcinomas in the ptcl-+/- mouse. Green and black tea. *Skin Pharmacology and Applied Skin Physiology*, **14**: 358-362.

Hibasami, H., Jin, Z.X., Hasegawa, M., Urakawa, K., Nakagawa, M., Ishii, Y., and Yoshioka, K. (2000). Oolong tea polyphenol extract induces apoptosis in human stomach cancer cells. *Anticancer Research*, **20**: 4403-4406.

Higashimoto, M., Akada, Y., Sato, M., Kinouchi, T., Kuwahara, T., and Ohnishi, Y. (2000) Inhibitory effects of tea extracts on the mutagenicity of 1-methyl-1,2,3,4-tetrahydro-beta-carboline-3-carboxylic acid on treatment with nitrite in the presence of ethanol. *Food and Chemical Toxicology*, **38**: 7-13.

Higginson, J. (1966). Etiological factors in gastrointestinal cancer in man. *Journal of the National Cancer Institute*, **37**: 527-545.

Hirano, S., Muto, R., Ikeda, T., and Watanabe, M. (2002). Effect of catechin inhalation therapy on control of MRSA. *Nippon Byoin Yakuzaishikai Zasshi*, **38**: 441-442.

Hirose, M., Hoshiya, T., Mizoguchi, Y., Nakamura, A., Akagi, K., and Shirai, T. (2001). Green tea catechins enhance tumor development in the colon without effects in the lung or thyroid after pretreatment with 1,2-dimethylhydrazine or 2,2'-dihydroxy-di-n-propylnitrosamine in male F344 rats. *Cancer Letters*, **168**: 23-29.

Hodgson, J.M., Puddey, I.B., Mori, T.A., Burke, V., Baker, R.I., and Beilin, L.J. (2001).Effect of regular ingestion of black tea on haemostasis and cell adhesion molecules in humans. *European Journal of Clinical Nutrition*, **55**: 881-886.

Hong, J.T., Ryu, S.R., Kim, H.J., Lee, J.K., Lee, S.H., Kim, D.B., Yun, Y.P., Ryu, J.H., Lee, B.M., and Kim P.Y. (2000). Neuroprotective effect of green tea extract in experimental ischemia-reperfusion brain injury. *Brain Research Bulletin*, **53**: 743-749.

Hong, J.T., Ryu, S.R., Kim, H.J., Lee, J.K., Lee, S.H., Yun, Y.P., Lee, B.M., and Kim, P.Y. (2001). Protective effect of green tea extract on ischemia/reperfusion-induced brain injury in Mongolian gerbils. *Brain Research*, **888**: 11-18.

Horie, H., Nesumi, A., Ujihara, T., and Kohata, K. (2002). Rapid determination of caffeine in tea leaves. *Journal of Chromatography*, **942**: 271-273.

Hosoda, K., Wang, M.F., Liao, M.L., Chuang, C.K., Iha, M., Clevidence, B., and Yamamoto, S. (2003). Antihyperglycemic effect of oolong tea in type 2 diabetes. *Diabetes Care*, **26**: 1714-1718.

Hsu, Y.W., Tsai, C.F., Chen, W.K., Huang, C.F., and Yen, C.C. (2011) A. subacute toxicity evaluation of green tea (*Camellia sinensis*) extract in mice. *Food and Chemical Toxicology*, **49**: 2624-3260.

Hu, XiuFang, Yang, XianQiang, Chen, LiuJi, Zhu, ShanJin, Hong, ZongYuan, Song, JianGuo and Sun, RuiYuan (2000). Effect of tea polyphenols on kidney disorder of rabbit. *Journal of Tea Science*, **20**: 148-154.

Hung, Y.C., Sava, V.M., Juang, C.L., Yeh, T.C., Shen, W.C., and Huang, G.S. (2002).Gastrointestinal enhancement of mri with melanin derived from tea leaves (*Thea sinensis* Linn.). *Journal of Ethnopharmacology*, **79**: 75-79.

Islam, M.S. (2011). Effects of the aqueous extract of white tea (*Camellia sinensis*) in a streptozotocin-induced diabetes model of rats. *Phytomedicine*, **19**: 25-31.

Jia, X.D., and Han, C. (2000) Chemoprevention of tea on colorectal cancer induced by dimethylhydrazine in Wistar rats. *World Journal of Gastroenterology*, **6**: 699-703.

Jiang, T., Glickman, B.W., and De Boer, J.G. (2001). Protective effect of green tea against benzo[alpha]pyrene-induced mutations in the liver of big blue transgenic mice. *Mutation Research*, **48**: 147-151.

Kang, J.H., Chung, S.T., Go, J.H., and Row, K.H. (2000). Separation of epigallocatechin gallate from Korean green tea by RP-HPLC. *Journal of Liquid Chromatography*, **23**: 2739-2749.

Kang, W.S., Chung, K.H., Chung, J.H., Lee, J.Y., Park, J.B., Zhang, Y.H., Yoo, H.S., and Yun Y.P. (2001). Antiplatelet activity of green tea catechins is mediated by inhibition of cytoplasmic calcium increase. *Journal of Cardiovascular Pharmacology*, **38**: 875-884.

Katiyar, S.K., and Mukhtar, H. (1997). Tea antioxidants in cancer chemoprevention. *Journal of Cellular Biochemistry*, **27**: 59-67.

Kennedy, D.O., Kojimaa, A., Yanob, Y., Hasumab, Otanib, S., and Matsui-Yuasaa, I. (2001). Growth inhibitory effect of green tea extract in Ehrlich ascites tumor cells involves cytochrome c release and caspase activation. *Cancer Letters*, **166**: 9-15.

Keya, C.A., Crozier, A., and Ashihara, H. (2003). Inhibition of caffeine biosynthesis in tea (*Camellia sinensis*) and coffee (*Coffea arabica*) plants by ribavirin. *FEBS Letters*, **554**: 473-477.

Kim, Y., Goodner, K.L., Park, J.D., Choib, J., and Talcottc, S. (2011). Changes in antioxidant phytochemicals and volatile composition of *Camellia sinensis* by oxidation during tea fermentation. *Food Chemistry*, **129**: 1331-1342.

Klein, R.D., and Fischer, S.M. (2002). Black tea polyphenols inhibit igf-i-induced signaling through akt in normal prostate epithelial cells and du145 prostate carcinoma. *Carcinogenesis*, **23**: 217-221.

Kobayashi, K., Teruya, T., Suenaga, K., Matsui, Y., Masuda, H., and Kigoshi, H. (2006). Isotheasaponins B1–B3 from *Camellia sinensis* var. *sinensis* tea leaves. *Phytochemistry*, **67**: 1385-1389.

Kojima-Yuasa, A., Hua, J.J., Kennedy, D.O., and Matsui-Yuasa, I. (2003). Green tea extract inhibits angiogenesis of human umbilical vein endothelial cells through reduction of expression of VEGF receptors. *Life Sciences*, **73**: 1299-1213.

Koshiishi, C., Kato, A., Yama, S., Crozier, A., and Ashihara, H. (2001). A new caffeine biosynthetic pathway in tea leaves: utilization of adenosine released from the *S*-adenosyl-*L*-methionine cycle. *FEBS Letters*, **499**: 50-54.

Krahwinkel, T., and Willershausen, B. (2000). The effect of sugar-free green tea chew candies on the degree of inflammation of the gingiva. *European Journal of Medical Research*, **5**: 463-467.

Krul, C., Luiten-Schuite, A., Tenfelde, A., van Ommen, B., Verhagen, H., and Havenaar, R. (2001). Antimutagenic activity of green tea and black tea extracts studied in dynamic *in vitro* gastrointestinal model. *Mutatation Research*, **474**: 71-85.

Lakenbrink, C., Lam, T.M., Engelhardt, U.H., and Wray, V. (2000). New flavonol triglycosides from tea (*Camellia sinensis*). *Natural Product Letters*, **14**: 223-238.

Lambert, J.D., Kennett, M.J., Sang, S., Reuhl, K.R., Ju, J., and Yang, C.S. (2010). Hepatotoxicity of high oral dose (-)-epigallocatechin-3-gallate in mice. *Food and Chemical Toxicology*, **48**: 409-416.

Langley-Evans, S.C. (2000). Consumption of black tea elicits an increase in plasma antioxidant potential in humans. *International Journal of Food Sciences and Nutrition*, **51**: 309-315.

Leung, L.K., Su, Y., Chen, R., Zhang, Z., Huang, Y., and Chen, Z.Y. (2001). Theaflavins in black tea and catechins in green tea are equally effective antioxidants. *Journal of Nutrition*, **131**: 2248-2251.

Levites, Y., Youdim, B.H., Maor, G., and Mandel, S. (2002). Attenuation of 6-hydroxydopamine (6-OHDA)-induced nuclear factor-kappa-b (NF-kappa-B) activation and cell death by tea extracts in neuronal cultures. *Biochemical Pharmacology,* **63**: 21-29

Li, N., Chen, X., Liao, J., Yang, G., Wang, S., Josephson, Y., Han, C., Chen, J., Huang, M.T., and Yang, C.S. (2002). Inhibition of 7,12-dimethylbenz[a]anthracene (DMBA)-induced oral carcinogenesis in hamsters by tea and curcumin. *Carcinogenesis*, **23**: 1307-1313.

Li, N., Ma, Z.J., Chu, Y., Wang, Y., and Li, X. (2013). Phytochemical analysis of the triterpenoids with cytotoxicity and QR inducing properties from the total tea seed saponin of *Camellia sinensis*. *Fitoterapia,* **84**: 321-325.

Liu, S.J., Zhang, N.X., and Yang, H. (2000). Induction of apoptosis in human hepatoma cells by green tea catechins. *Chinese Journal of Clinical Oncology,* **27**: 902-905.

Loest, H.B., Noh, S.K., and Koo, S.I. (2002). Green tea extract inhibits the lymphatic absorption of cholesterol and alpha-tocopherol in ovariectomized rats. *Journal of Nutrition*, **132**: 1282-1288.

Lu, Y., Umeda, T., Yagi, A., Sakata, K., Chaudhuri, T., Ganguly, D.K., and Sarma, S. (2000). Triterpenoid saponins from the roots of tea plant (*Camellia sinensis* var. *assamica*). *Phytochemistry*, **53**: 941-946.

Lu, Y.P., Lou, Y.R., Lin, Y., Shih, W.J., Huang, M.T., Yang, C.S., and Conney, A.H. (2001). Inhibitory effects of orally administered green tea, black tea, and caffeine on skin carcinogenesis in mice previously treated with ultraviolet B light (high-risk mice): relationship to decreased tissue fat. *Cancer Research*, **61(13)**: 5002-5009.

Luo, Z.M., Ling, T.J., Li, L.X., Zhang, Z.Z., Zhu, H.T., Zhang, Y.J., and Wan, X.C. (2012). A new norisoprenoid and other compounds from fuzhuan brick tea. *Molecules,* **17**: 3539-3546.

Maity, S., Vedasiromoni, Jr., Chaudhuri, L., and Ganguly, D.K. (2001). Role of reduced glutathione and nitric oxide in the black tea extract-mediated protection against ulcerogen-induced changes in motility and gastric emptying in rats. *Japanese Journal of Pharmacology*, **85**: 358-364.

Maliakal, P.P., Coville, P.F., and Wanwimolruk, S. (2001). Tea consumption modulates hepatic drug metabolizing enzymes in Wistar rats. *Journal of Pharmacy and Pharmacology*, **53**: 569-577.

Manir, M.M., Kim, J.K., Lee, B.G., and Moon, S.S. (2012). Tea catechins and flavonoids from the leaves of *Camellia sinensis* inhibit yeast alcohol dehydrogenase. *Bioorganic and Medicinal Chemistry*, **20**: 2376-2381.

Mao, L.G., and Yu, J.X. (2000). Effect of tea extract on dispelling alcoholic intoxication in mice. *Chaye Kexue*, **20**: 155-157.

Marnewick, J.L., Joubert, E., Swart, P., Van Der Westhuizen, F., and Gelderblom, W.C. (2003). Modulation of hepatic drug metabolizing enzymes and oxidative status by rooibos (*Aspalathus linearis*) and honeyhush (*Cyclopia intermedia*), green and black (*Camellia sinensis*) teas in rats. *Journal of Agricultural and Food Chemistry,* **51**: 8113-8119.

Marnewick, J.L., van der Westhuizen, F.H., Joubert, E., Swanevelder, S., Swart, P., and Gelderblom, W.C. (2009). Chemoprotective properties of rooibos (*Aspalathus linearis*), honeybush (*Cyclopia intermedia*) herbal and green and black (*Camellia sinensis*) teas against cancer promotion induced by fumonisin B1 in rat liver. *Food and Chemical Toxicology*, **47**: 220-229.

Maron, D.J., Lu, G.P., Cai, N.S., Wu, Z.G., Li, Y.H., Chen, H., Zhu, J.Q., Jin, X.J., Wouters, B.C., and Zhao, J. (2003). Cholesterol-lowering effect of a theaflavin-enriched green tea extract. *Archives of Internal Medicine*, **163**: 1448-1453.

Matsubara, S., Shibata, H., Ishikawa, F., Yokokura, T., Takahashi, M., Sugimura, T., and Wakabayashi, K. (2003). Suppression of *Helicobacter pylori*-induced gastritis by green tea extract in Mongolian gerbils. *Biochemical and Biophysical Research Communication*, **310**: 715-719.

Mauri, P., and Pietta, P. (2000). Electrospray characterization of selected medicinal plant extracts. *Journal of Pharmaceutical and Biomedical Analysis*, **23**: 61-68.

Melzig, M.F., and Janka, M. (2003). Enhancement of neutral endopeptidase activity on SK-N-SH cells by green tea extract. *Phytomedicine*, **10**: 494-498.

Metz, N., Lobstein, A., Schneider, Y., Gossé, F., Schleiffer, R., Anton, R., and Raul, F. (2000). Suppression of azoxymethane-induced preneoplastic lesions and inhibition of cyclooxygenase-2 activity in the colonic Mucosa of rats drinking a crude green tea extract. *Nutrition and Cancer*, **38**: 60-64.

Mondal, T.K., Bhattacharya, A., Laxmikumaran, M., and Ahuja, P.S. (2004) Recent advances of tea (*Camellia sinensis*) biotechnology. *Plant Cell Tissue and Organ Culture,* **76**: 195-254.

Mukoda, T., Sun, B., and Ishiguro, A. (2001). Antioxidant activities of buckwheat hull extract toward various oxidative stress *in vitro* and *in vivo*. *Biological and Pharmaceutical Bulletin*, **24**: 209-213.

Murakami, T., Nakamura, J., Kageura, T., Matsuda, H., and Yoshikawa, M. (2000). Bioactive saponins and glycosides. XVII. Inhibitory effect on gastric emptying

and accelerating effect on gastrointestinal Transit of tea saponins: structures of assamsaponins F, G, H, I, and J from the seeds and leaves of the tea plant. *Chemical and Pharmaceutical Bulletin*, **48**: 1720-1725.

Nakagawa, T., Yokozawa, T., Terasawa, K., Shu, S., and Juneja, L.R. (2002). Protective activity of green tea against free radical- and glucose-mediated protein damage. *Journal of Agricultural and Food Chemistry*, **50**: 2418-2422.

Paganini-Costa, P., and Carvalho-da-Silva, D. (2011). A cup (tea) of chemistry. *Revista Virtual Quimica*, **3**: 27-36.

Pastore, R.L., and Fratellone, P. (2006). Potential health benefits of green tea (*Camellia sinensis*): a narrative review. *Diet and Nutrition*, **2**: 531-539.

Peters, U., Poole, C., and Arab, L. (2001). Does tea affect cardiovascular disease? A meta-analysis. *American Journal of Epidemiology*, **154**: 495-403.

Pietta, P., Simonetti, P., Gardana, C., and Mauri, P. (2000). Trolox equivalent antioxidant capacity (TEAC) of *Ginkgo biloba* flavonol and *Camellia sinensis* catechin metabolites. *Journal of Pharmaceutical and Biomedical Analysis*, **23**: 223-226.

Pisters, K.M., Newman, R.A., Coldman, B., Shin, D.M., Khuri, F.R., Hong, W.K., Glisson, B.S., and Lee, J.S. (2001). Phase I trial of oral green tea extract in adult patients with solid tumors. *Journal of Clinical Oncology*, **19**: 1830-1838.

Pressentin, M.D.M., Chen, M., and Guttenplan, J.B. (2001). Mutagenesis induced by 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone-4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone and n-nitrosonorinicotine in lacz upper aerodigestive tissue and liver and inhibition by green tea. *Carcinogenesis*, **122**: 203-206.

Qin, G.Z., Ning, Y.Y., and Lotlikar, P.D. (2000). Chemoprevention of aflatoxin B-1-initiated and carbon tetrachloride-promoted hepatocarcinogenesis in the rat by green tea. *Nutrition and Cancer,* **38**: 215-222.

Rao, G.Y., Chem, X.F., Yu, Y.N., and Liu, Q.L. (2000). Protective effects of tea pigment on experimental liver injury in mice. *Zhongguo Yaoxue Zazhi*, **35**: 813-815.

Ratnasooriya, W.D., and Fernando, T.S.P. (2008). Effect of black tea brew of *Camellia sinensis* on sexual competence of male rats. *Journal of Ethnopharmacology*, **118**: 373-377.

Richelle, M., Tavazzi, I., and Offord, E. (2001). Comparison of the antioxidant activity of commonly consumed polyphenolic beverages (coffee, cocoa, and tea) prepared per cup serving. *Journal of Agricultural and Food Chemistry*, **49**: 3438-3442.

Robb, C.S., Geldart, S.E., Seelenbinder, J.A., and Brown, P.R. (2002). Analysis of green tea constituents by HPLC-FTIR. *Journal of Liquid Chromatography and Related Technologies*, **25**: 787-801.

Rusak, G., Komes, D., Likic S, Horžic, D., and Kovaè, M. (2008). Phenolic content and antioxidative capacity of green and white tea extracts depending on extraction conditions and the solvent used. *Food Chemistry*, **110**: 852-858.

Sabu, M.C., Smitha, K., and Kuttan, R. (2002). Anti-diabetic activity of green tea polyphenols and their role in reducing oxidative stress in experimental diabetes. *Journal of Ethnopharmacology*, **83**: 109-116.

Samman, S., Sandström, B., Toft, M.B., Bukhave, K., Jensen, M., Sørensen, S.S., and Hansen, M. (2001). Green tea or rosemary extract added to foods reduces nonheme-iron absorption. *American Journal of Clinical Nutrition*, **173**: 607-612.

Santana, M.B., Mandarino, M.G., Cardoso, J.R., Dichi, I., Dichi, J.B., Camargo, A.E., Fabris, B.A., Rodrigues, R.J., Fatel, E.C., Nixdorf, S.L., Simão, A.N., Cecchini, R., and Barbosa, D.S. (2008). Association between soy and green tea (*Camellia sinensis*) diminishes hypercholesterolemia and increases total plasma antioxidant potential in dyslipidemic subjects. *Nutrition*, **24**: 562-568.

Sarkar, A., and Bhaduri, A. (2001). Black tea is a powerful chemopreventor of reactive oxygen and nitrogen species: comparison with its individual catechin constituents and green tea. *Biochemical and Biophysical Research Communications*, **284**: 173-178.

Sartippour, M.R., Heber, D., Zhang, L., Beatty, P., Elashoff, D., Elashoff, R., Go, V.L., and Brooks, M.N. (2002). Inhibition of fibroblast growth factors by green tea. *International Journal of Oncology*, **21**: 487-491.

Schmitz, W.O., Cecchini, R., Estevão, D., and Saridakis, H.O. (2009). Hepatic protection effect of the alcoholic extract from *Camellia sinensis* (L.) Kuntze (green tea) in Wistar rats treated with diethylnitrosamine. *Brazilian Journal of Pharmacognosy*, **19**: 702-709.

Scoparo, C.T., Souza, L.M., Dartora, N., Sassaki, G.L., Gorin, P.A., and Iacomini, M. (2012). Analysis of *Camellia sinensis* green and black teas via ultra high performance liquid chromatography assisted by liquid–liquid partition and two-dimensional liquid chromatography (size exclusion × reversed phase). *Journal of Chromatography A*, **1222**: 29-37.

Setiawan, V.W., Zhang, Z.F., Yu, G.P., Lu, Q.Y., Li, Y.L., Lu, M.L., Wang, M.R., Guo, C.H., Yu, S.Z., Kurtz, R.C., and Hsieh, C.C. (2001). Protective effect of green tea on the risks of chronic gastritis and stomach cancer. *International Journal of Cancer*, **92**: 600-604.

Sharangi, A.B. (2009). Medicinal and therapeutic potentialities of tea (*Camellia sinensis* L.) – A review. *Food Research International*, **42**: 529-535.

Sharma, A., Gupta, S., Sarethy, I.P., Dang, S., and Gabrani, R. (2012). Green tea extract: possible mechanism and antibacterial activity on skin pathogens. *Food Chemistry*, **135**: 672-675.

Sharquie, K., Al Turfi, I.A., and Al Salloum, S.M. (2000). The antibacterial activity of tea *in vitro* and *in vivo* (in patients with *Impetigo contagiosa*). *Journal of Dermatology*, **27**: 706-710.

Shukla, Y., and Taneja, P. (2001). Antimutagenic effect of black tea extract using 'rodent dominant lethal mutation assay'. *Toxicology*, **168**: 269-274.

Shukla, Y., and Taneja, P. (2002). Anticarcinogenic effect of black tea on pulmonary tumors in Swiss albino mice. *Cancer Letters*, **176**: 137-141.

Soares, M.B., Izaguirry A.P., Vargas L.M., Mendez, A.S., Spiazzi, C.C., and Santos, F.W. (2013). Catechins are not major components responsible for the beneficial effect of *Camellia sinensis* on the ovarian d-ALA-D activity inhibited by cadmium. *Food Chemical and Toxicology*, **55**: 463-469.

Steele, V.E., Kelloff, G.J., Balentine, D., Boone, C.W., Mehta, R., Bagheri, D., Sigman, C.C., Zhu, S., and Sharma, S. (2000). Comparative chemopreventive mechanisms of green tea, black tea and selected polyphenol extracts measured by *in vitro* bioassay. *Carcinogenesis*, **21**: 63-67.

Suganuma, M., Ohkura, Y., Okabe, S., and Fujiki, H. (2001). Combination cancer chemoprevention with green tea extract and sulindac shown in intestinal tumor formation in min mice. *Journal of Cancer Research and Clinical Oncology*, **127**: 69-72.

Sung, H., Nah, J., Chun, S., Park, H., Yang, S.E., and Min, W.K. (2000). *In vivo* antioxidant effect of green tea. *European Journal of Clinical Nutrition*, **54**: 527-529.

Sur, P., and Ganguly, D.K. (1994). Tea plant root extract (TRE) as an antineoplastic agent. *Planta Medica,* **60**: 106-109.

Tachibana, H., Sunada, Y., Miyase, T., Sano, M., Maeda-Yamamoto, M., and Yamada, K. (2000). Identification of a methylated tea catechin as an inhibitor of degranulation in human basophilic KU812 cells. *Bioscience, Biotechnology and Biochemistry*, **64**: 452-454.

Tanaka, T., Betsumiya, Y., Mine, C., and Kouno, I. (2000). Theanaphthoquinone, a novel pigment oxidatively derived from theaflavin during tea-fermentation. *Chemical Communications*, 1365-1366.

Terahara, N., Takeda, Y., Nesumi, A., and Honda, T. (2001). Anthocyanins from red flower tea (Benibana-cha), *Camellia sinensis*. *Phytochemistry*, **56**: 359-361.

Thiagarajan, G., Chandani, S., Sundari, C.S., Rao, S.H., Kulkarni, A.V., and Balasubramanian, D. (2001). Antioxidant properties of green and black tea, and their potential ability to retard the progression of eye lens cataract. *Experimental Eye Research*, **73**: 393-401.

Tomita, M., Yamamoto, S., Yamaguchi, K., Ohigashi, H., Yagi, T., Kohata, K., and Berden, J.A. (2000). Theasaponin E-1 destroys the salt tolerance of yeasts. *Journal of Bioscience and Bioengineering*, **90**: 637-642.

Tsai, C.F., Hsu, Y.W., Ting, H.C., Huang, C.F., and Yen C.C. (2013). The *in vivo* antioxidant and antifibrotic properties of green tea (*Camellia sinensis*, Theaceae). *Food Chemistry*, **136**: 1337-1344.

Uehara, M., Sugiura, H., and Sakurai, K. (2001). A trial of oolong tea in the management of recalcitrant atopic dermatitis. *Archives of Dermatology*, **137**: 42-43.

Uesato, S., Kitagawa, Y., Kamishimoto, M., Kumagai, A., Hori, H., and Nagasawa, H. (2001). Inhibition of green tea catechins against the growth of cancerous human colon and hepatic epithelial cells. *Cancer Letters*, **170**: 41-44.

Umashankar, D.C. (2001). Quantitative and qualitative analysis of (-)-Epigallocatechin gallate from green tea by LC-MS. *Journal of Natural Remedies*, **1**: 151-154.

Vaijayanthimala, J., Anandi, C., Udhaya, V., and Pugalendi, K.V. (2000). Anticandidal activity of certain South Indian medicinal plants. *Phytotherapy Research*, **14**: 207-209.

van der Merwe, J.D., Joubert, E., Richards, E.S., Manley, M., Snijman, P.W., Marnewick, J.L., and Gelderblom, W.C. (2006). A comparative study on the antimutagenic properties of aqueous extracts of *Aspalathus linearis* (rooibos), different *Cyclopia* spp. (honeybush) and *Camellia sinensis* teas. *Mutation Research*, **611**: , 42-53.

Vitaglione, P., Morisco, F., Caporaso, N., and Fogliano, V. (2004). Dietary antioxidant compounds and liver health. *Critical Reviews in Food Science and Nutrition*, **44**: 575-586.

Wada, S., He, P., Hashimoto, I., Watanabe, N., and Sugiyama, K. (2000). Glycosidic flavonoids as rat-liver injury preventing compounds from green tea. *Bioscience, Biotechnology and Biochemistry*, **64**: 2262-2265.

Wei, K., Wang, L., Zhou, J., He, W., Zeng, J., Jiang, J., and Cheng, H. (2011).Catechin contents in tea (*Camellia sinensis*) as affected by cultivar and environment and their relation to chlorophyll contents. *Food Chemistry*, **125**: 44-48.

Xu, R., Ye, H., Sun, Y., Tub, Y., and Zenga, X. (2012). Preparation, preliminary characterization, antioxidant, hepatoprotective and antitumor activities of polysaccharides from the flower of tea plant (*Camellia sinensis*). *Food and Chemical Toxicology*, **50**: 2473-2480.

Xu, Y., Chen, X.B., and Xiao, W.X. (2002). Preparation and application of theanine. *Tianran Chanwu Yanjiu Yu Kaifa*, **14**: 77-80.

Xuan, W.L., Wang, S.W., Han, C., and Chen, J.S. (2000) Preventive effects of tea pigment on experimental atherosclerosis in hypercholesterolemia rabbits. *Zhongguo Dongmai Yinghua Zazhi*, **8**: 131-133.

Xuan, W.L., Wang, S.W., Han, C., and Chen, J.S. (2001). Study on inhibition of tea pigments on adhesion between monocyte and endothelial cells. *Weisheng Yanjiu,* **30**: 44-46.

Yang, C.S., Lambert, J.D., Ju, J., Lu, G., and Sang, S. (2007). Tea and cancer prevention: molecular mechanisms and human relevance. *Toxicology and Applied Pharmacology*, **224**: 265-273.

Yang, F.J., Oz, H.S., Barve, S., De Villiers, W.J.S., Mcclain C.J., and Varilek, G.W. (2001). The green tea polyphenol (-)-epigallocatechin-3-gallate blocks nuclear factor-KAPPA B activation by inhibiting 1-KAPPA B kinase activity in the intestinal epithelial cell line IEC-6. *Molecular Pharmacology*, **60**: 528-533.

Yang, T.T.C., and Koo, M.W.L. (2000). Inhibitory effect of Chinese green tea on endothelial cell-induced LDL oxidation. *Atherosclerosis*, **148**: 67-73.

Yee, Y.K. and Koo, M.W.L. (2000). Anti-helicobacter pylori activity of Chinese tea: *in vitro* study. *Alimentary Pharmacology and Therapeutics,* **14**: 635-638.

Yildirim, A., Mavi, A., Oktay M., Kara, A.A., Algur, O.F., and Bilaloglu, V. (2000). Comparison of antioxidant and antimicrobial activities of tilia (*Tilia argentea* Desf ex DC), sage (*Salvia triloba* L.), and black tea (*Camellia sinensis*) extracts. *Journal of Agricultural and Food Chemistry,* **48**: 5030-5034.

Yokozawa, T., Cho, E.J., Nakagawa, T., and Terasawa, K. (2000). Inhibitory effect of green tea tannin on free radical-induced injury to the renal epithelial cell line, LLC-PK-1. *Pharmacy and Pharmacology Communications,* **6**: 521-526.

Zhang, G.Y., Miura, Y., and Yagasaki, K. (2002). Effects of dietary powdered green tea and theanine on tumor growth and endogenous hyperlipidemia in hepatomabearing rats. *Bioscience, Biotechnology, and Biochemistry*, **66**: 711-716.

Zhang, G.Y., Miura, Y., and Yagasaki, K. (2000). Induction of apoptosis and cell cycle arrest in cancer cells by *in vivo* metabolites of teas. *Nutrition and Cancer*, **38**: 265-273.

Zhang, Y., Li, S.M., Lin, Z., and Yin, D. (2001). Separation and determination of chlorogenic acid in green tea for medicinal component. *Shipin Kexue*, **22**: 86.

Zhou, C.Y., and Peng, J.D. (2002). Determination of theanine in tea leaves by HPLC-inhibited chemiluminescence with Co^{2+} catalyst. *Chinese Journal of Chromatography*, **20**: 550-553.

Zhou, Z.H., and Yang, C.R. (2000). Chemical constituents of crude green tea, the material of puer tea in Yunnan. *Yunnan Zhiwu Yanjiu,* **22**: 343-350.