21 Preventive and Therapeutic Effects of Plant Polyphenols through Suppression of Nuclear Factor-Kappa B

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CONTENTS

21.1 OVERVIEW

Nuclear transcription factor-κB (NF-κB) regulates the expression of over 200 different genes. The activation of NF-κB has now been linked with a variety of inflammatory diseases, including cancer, atherosclerosis, myocardial infarction, diabetes, allergy, asthma, arthritis, Crohn's disease, multiple sclerosis, Alzheimer's disease, osteoporosis, psoriasis, septic shock, and AIDS. There is much evidence suggesting that phytochemicals can inhibit the pathways that lead to the activation of this transcription factor and have the potential to prevent and treat the diseases mentioned. These phytochemicals are derived from plants such as turmeric, red pepper, cloves, ginger, cumin, anise and fennel, rosemary, garlic, green tea, basil, cauliflower, cabbage, artichoke, lemon, and pomegranate.

21.2 INTRODUCTION

Plant extracts and natural compounds purified from plants have been used by humans for many centuries for the treatment and alleviation of a variety of inflammation-related diseases, including cancer. Eastern medicine, viz., traditional Chinese medicine (TCM) and the Indian ayurvedic system of medicine, continue to prescribe complex mixtures of herbs and herbal extracts for the treatment of cancer. Recent research has shown that a mechanism-based approach that targets the means by which cancer cells prosper has significant advantages over the current methods of cancer treatment, including chemotherapy, with their attendant adverse effects. The regulation of the cell cycle (cell survival, proliferation, and death) requires the integration of a myriad of cell-signaling factors, including those that direct the transcription of genes coding for integral cell proteins. Nuclear factor (NF)-κB is a transcription factor that regulates the expression of genes involved in cancer and other diseases.

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21.3 NF-κB AND DISEASE

NF-κB, discovered by David Baltimore in 1986, is a ubiquitous factor that resides in the cytoplasm in an inactive state. When activated, it is translocated to the nucleus and induces gene transcription. NF-κB is activated by free radicals, inflammatory stimuli, carcinogens, tumor promoters, endotoxins, gamma radiation, UV light, and x-rays. On activation, it induces the expression of more than 200 genes, and these genes have been shown to suppress apoptosis and induce cellular transformation, proliferation, invasion, metastasis, chemoresistance, radioresistance, and inflammation.[1–3] The activated form of NF-κB has been found to mediate cancer,[1,4,5] atherosclerosis,[6] myocardial infarction,[7] diabetes,[8] allergy,[9,10] asthma,[11] arthritis,[12] Crohn's disease,[13] multiple sclerosis,[14] Alzheimer's disease,[15,16] osteoporosis, psoriasis, septic shock, AIDS, and other inflammatory diseases[17–19] (Figure 21.1). That NF-κB has been linked to wide variety of diseases is not too surprising because most diseases are caused by dysregulated inflammatory mechanisms.[20] Thus, agents that can suppress NF-κB activation can, in principle, either prevent, delay the onset, or treat NF-κB -linked diseases.

Ever since research has shown that there is an intrinsic link between inflammation and various diseases, it has become obvious that inhibition of NF-κB activity is desirable in the treatment of not only inflammation but also the disease itself. For instance, aberrant NF-κB activation is a known factor in oncogenesis, tumor growth, and metastasis, and specific constitutive activation of NF-κB has been identified in a number of cancers including, breast, ovarian, colon, and prostate cancer and Hodgkin's lymphoma (for references see Reference 1). Hence, AU: Chapter title needs to be reduced in running head to fit. Pls. check wording.

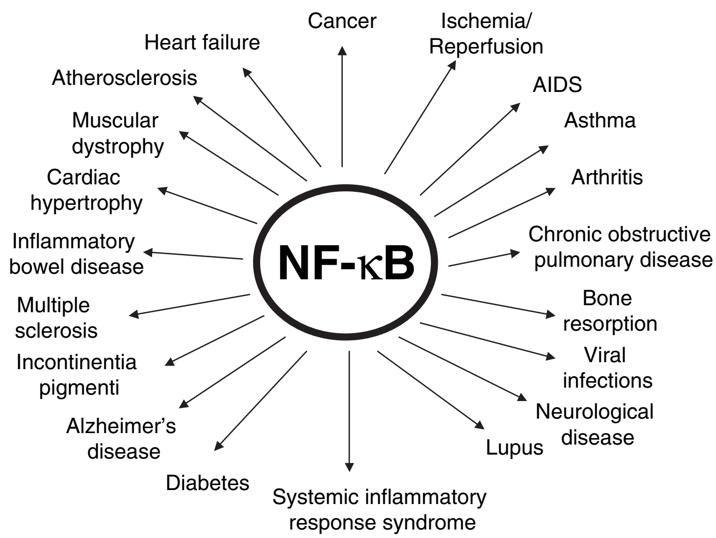

FIGURE 21.1 NF-κB-linked diseases.

this transcription factor is an important target in the prevention of diseases and their treatment in humans.

21.4 NF-κB AS A THERAPEUTIC TARGET

NF-κB represents an important and very attractive therapeutic target for plant-derived polyphenols. Much attention has been paid in the last decade to the identification of compounds that selectively interfere with this pathway. More recently, a great number of plant-derived natural products have been evaluated as possible inhibitors of the NF-κB pathway (Table 21.1, Figure 21.2). This chapter focuses on plant extracts, plant isolates, and distinct classes of plant-derived compounds that form part of this group. It is noteworthy that there are also reports of synthetic compounds and compounds from nonplant sources (e.g., caffeic acid phenethyl ester [CAPE] identified from honey bee propolis) that are known to block the activity of NF-κB[21].

NF-κB plays a central role in inflammation, and research has made it clear that most diseases are linked to inflammation. Because NF-κB can also regulate the expression of many key genes involved in a variety of human cancers, it represents a relevant and promising target for new therapeutic agents. Many pharmaceutical and biotechnology companies have drug discovery programs that target NF-κB and have been investing heavily in the search for proteins that regulate this transcription factor. However, due to the ubiquitous nature of NF-κB, many of these drugs may exhibit undesirable side effects.

The mechanism-based approach to combat diseases from different angles with combinations of naturally derived compounds has a distinct advantage in

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TABLE 21.1
Natural Products from Plants that Exhibit Chemopreventive and Therapeutic Activities against Cancer

Compound	Source	Botanical Name	Structure	↓NF-κB	P	T	Ref.
Polyphenol							
Amentoflavone (biapigenin)*	Gingko	*Gingko biloba; Cypress* spp.; *Galeobdolon chinense; Garcinia intermedia; Selaginella* spp.; *Biophytum sensitivum*		+	—	—	22,23
Apigenin*	Fruits and vegetables	*Scutellaria* spp. (incl. in Chinese herbal mixture, PCSPES, *Huang-Qi; Qingkailing; Shuanghuanglian etc.); Cirisium* spp.; *Crotalaria* spp.; *Quercus nutgall;Matricaria recutita; Saussurea medusa; Lantana montevidensis Briq.*	4′,5,7-Trihydroxyflavone	+	—	—	24–26
Arctigenin* and demethyltraxillagenin		*Arctium lappa; Centaurea* spp.; *Torreya nucifera*		+	—	—	27
Auraptene	Citrus fruits (hassaku, grapefruit, natudaidai)	*Citrus* spp.	7-Geranyl-oxycoumarin	—	—	—	28
Baicalein* and its derivatives[a]	Skullcap	*Scutellaria* spp. (included in Chinese herbal mixture, PCSPES, *Huang-Qi; Qingkailing; Shuanghuanglian, etc.)*	5,6,7-Trihydroxyflavone	+	+	+	29–31
Blueberry and berry mix	Blueberry, black currant, raspberry, strawberry	*Rubus* spp.; *Vaccinium* spp.; *Fragaria ananassa*		+	—	—	32–34
Cannabinol*	Hemp seed oil, marijuana	*Cannabis* spp.	6,6,9-Trimethyl-3-pentyl-6H-dibenzo[b,d]pyran-1-ol;	+	—	+	35–37

Catalposide*		*Catalpa* spp.; *Veronica* spp.	Oxireno[4,5]cyclopenta [1,2-c]pyran-β-*D*-glucopyranoside	+	—	—	38
Catechins* (and theaflavins*)[b]	Green tea (including fermented, i.e., black teas), spotted knapweed, shea kernels, cocoa	*Camellia sinensis; Centaurea maculosa; Vitellaria paradoxa; Theobroma cacao*	3′,4′,5,7-Tetrahydroxy-2,3-trans-flavan-3-ol	+	+	+	39–41
Cirsimaritin*	Basil, sage, rosemary	*Cirsium maritimum; Ocimum sanctum; Salvia officinalis; Rosmarinus officinalis*	5,4′-Dihydroxy-6,7-dimethoxyflavone	—	—	—	42
Curcumin*	Turmeric (*haldi*)	*Curcuma longa*	Diferuloylmethane	+	+	+	—
Ellagic acid*	Strawberries, raspberries, blackberries, bayberries, fuejioa, pomegranates, pineapple, walnuts	*Fragaria ananassa; Rubus idaeus;Punica granatum; Juglans regia*	4,4′,5,5′,6,6′-Hexahydroxy-diphenic acid dilactone	—	—	—	34,44
Emodin*	Aloe vera	*Polygonum* spp.; *Cassia* spp.; *Glossostemon bruguieri (moghat); Rheum* spp. *(rhubarb); Hovenia acerba*	3-Methyl-1,6,8-Trihydroxy-anthraquinone	+	+	—	45
Flavopiridol[c]			5,7-Dihydroxy-8-(4-*N*-methyl-2-hydroxypyridyl)-6′-chloroflavone hydrochloride	+	—	—	46
Genistein*	Soybeans, chickpea, kudzu root	*Glycine max; Cicer arietinum; Pueraria lobata radix; Desmodium* spp.	3-(4-Hydroxyphenyl)-5,7-dihydroxy-chromen-4-one	+	+	+	47,48
Glossogyne tenuifolia[d]	Herb	*Glossogyne tenuifolia*		+	—	—	49

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TABLE 21.1 (continued)
Natural Products from Plants that Exhibit Chemopreventive and Therapeutic Activities against Cancer

Compound	Source	Botanical Name	Structure	↓NF-κB	P	T	Ref.
Hematein*	Natural dye from logwood			+	—	—	50,51
Hesperidine	Oranges	*Citrus* spp.	Hesperitin-7-rutinoside	—	—	—	52
HMP*	Black fruit or galangal	*Alpinia* spp.	7-(4′-Hydroxy-3′-methoxyphenyl)-phenylheptenone	+	—	—	53
Hypericin*	St. John's wort	*Hypericum* spp.		+	+	+	54,55
Isothymusin	Basil	*Ocimum* spp.; *Limnophila geoffrayi; Becium grandiflorum*	6,7-Dimethoxy-5,8,4′-trihydroxyflavone	—	—	—	56
Isomallotochromanol* and isomallotochromene		*Mallotus japonicus*		+	—	—	57
Kaempferol	Fruits and vegetables e.g., tomato, onions	*Lycopersicon esculentum, Ginkgo biloba*	3,5,7,4′-Tetrahydroxyflavone	—	—	—	58
Luteolin*	Fruits and vegetables, tea	*Camellia sinensis; Scutellaria* spp.	2-(3,4-Dihydroxyphenyl)-5,7-dihydroxy-chromen-4-one	+	—	—	25,59
Morin	Guava, almond	*Psidium guajava; Prunus dulcis*	2′,3,4′,5,7-Pentahydroxy-flavone	—	+	+	60
Myricetin	Fruits and vegetables		2-(3,4-5-Trihydroxyphenyl)-3,5,7-Trihydroxy-chromen-4-one	—	—	—	61

Nasunin	Eggplant	*Solanum melongena*	Delphinidin-3-(*p*-coumaroylrutinoside)-5-glucoside	—	—	—	62
Nobiletin	Citrus	*Citrus* spp.	5,6,7,8,3′,4′-Hexamethoxy flavone	—	—	—	28
Nordihydroguaiaretic acid*		*Guaiacum officinale*		+	—	—	63
Ochna macrocalyx ext.		*Ochna macrocalyx*		+	—	—	64
Oenothein B		*Oenothera* spp.; *Eugenia uniflora*	Hydrolyzable ellagitannin	—	—	—	65
Panduratin A		*Kaempferia pandurata*		+	—	—	66
Procyanidins	Tea, cranberries, apple, grape seeds, pear	*Camellia sinensis, Vaccinum* spp.; *Prunus* spp.	Condensed tannins	—	—	—	67
Purpurogallin		*Quercus sp.* Nutgall	2,3,4,6-Tetrahydroxy-5H-bezocyclohepten-5-one	—	—	—	68,69
Pycnogenol	Maritime pine bark extract	*Pinus maritima*	Bioflavanoid extract	+	—	—	70,71
Quercetin	Fruits and vegetables	*Malus* spp.; *Lycopersicon esculentum*	2-(3,4-Dihydroxyphenyl)-3,5,7-trihydroxy-chromen-4-one	+	—	—	72
Rhein		*Daylilies (Hemerocallis* spp.*); Rheum officinale (dahuang)*	1,8-Dihydroxy-3-carboxyanthraquinone	+	—	—	73
Sanggenon C*	Mulberry	*Morus* spp.		+	—	—	74
Silymarin[e]	Milk thistle, artichokes	*Silybum marianum; Cynara scolymus*	Flavonolignan extract	+	+	+	75,76,77
Saucerneols*, sauchinone, and manassantins*		*Saururus* spp.		+	—	—	78,79
Tangeretin	citrus fruits	*Citrus* spp.	5,6,7,8,4′-Pentamethoxyflavone	—	—	—	80

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TABLE 21.1 (continued)
Natural Products from Plants that Exhibit Chemopreventive and Therapeutic Activities against Cancer

Compound	Source	Botanical Name	Structure	↓NF-κB	P	T	Ref.
Wedelolactone*		*Wedelia* spp.; *Eclipta alba*	1,8,9-Trihydroxy-3-methoxy-6H-benzofuro[3,2][1]-benzopyran-6-one,	+	—	—	81
Yakuchinones* A and B		*Alpinia oxyphylla*	1-(4′-Hydroxy-3′-methoxyphenyl)-7-phenyl-3-heptanone,1-(4′-hydroxy-3′-methoxyphenyl)-7-phenylhept-1-en-3-one	+	—	—	82
		Terpenes					
Andalusol*		*Siderites foetens*		+	—	—	83
Anethol*[f] and analogs	Broccoli, anise, cloves, cashew	*Brassica oleracea; Illicum verum; Ocimum* spp.; *Syzygium aromaticum; Anacardium occidentale; Hibiscus sabdariffa*	4-Methoxypropenylbenzene	+	+	+	84,85
Artemisinin (qinghaosu)		*Artemisia annua L.* spp.		+	—	—	86
Avicins*[g]		*Acasia victoriae*		+	—	—	87
Azadirachtin[h]	Neem tree	*Azadirachta indica, A. Jussieu*		—	—	—	88
β-carotene	Carrot, citrus fruits, pumpkin	*Daucus carota sativus; Citrus unshiu mar; Curcurbita moschata*		—	—	—	89,90
β-cryptoxanthin	Fruits	*Carica papaya L. Physalis*	β,β-Caroten-3-ol	—	—	—	89,91
Bakuchiol (drupanol)*	Bemchi seeds	*Psoralea corylifolia (bemchi); Otholobium pubescens*	4-(3-ethenyl-3,7-dimethyl-1,6-octadienyl)-phenol	+	—	—	92

Betulinic acid*	Birch tree, almond hulls	*Betula* spp.; *Quisqualis Fructus; Coussarea paniculata; Alangium lamarckii*	3-β-Hydroxy-1up-20(29)en-28-acid	+	—	—	93
Carnosol*	Rosemary, sage	*Rosmarinus officinalis; Salvia officinalis*	2H-9,4a-(epoxymethano)-phenanthren-12-one	+	—	—	94
Celastrol*		*Celastrus orbiculatus*		+	—	—	95
Costunolide*		*Magnolia grandiflora; Tsoongiodendron odorum; Saussurea lappa*		+	—	—	96
Cucurbitacins[i]	Cucurbitaceae	*Cucurbita andreana; Trichosanthes kirilowii; Elaeocarpus mastersii*	3-β-(β-*D*-Glucosyloxy)-16-,23-α-epoxycucurbita-5,24-diene-11-one	—	—	—	97,98
Ergolide*		*Inula* spp.	Dihydrobigelovin	+	—	—	99
Excisanin A*		*Isodon (Rabdosia)* spp.		+	—	—	100
Foliol*		*Sideritis* spp.		+	—	—	101
Germacranolides *[j] and Eudesmanolides		*Carpesium divaricatum; Montanoa hibiscifolia*		+	—	—	102,103
Ginkgo biloba ext.		*Gingko biloba*		+	—	—	104
Ginsenoside Rg3*		*Panax* spp.		+	—	—	105
Glycyrrhizin*	Licorice root	*Glycyrrhiza glabra; Glycyrrhiza uralens*		+	—	—	106
Guaianolides*		*Viguiera gardneri*		+	—	—	107
Helenalin*		*Arnicae* spp.; *Helenium aromaticum*		+	—	—	108
Hypoestoxide		*Hypoestes rosea*		+	—	—	109,110
Kamebacetal A*		*Isodon (Rabdosia)* spp.		+	—	—	100
Kamebakaurin		*Isodon (Rabdosia)* spp.		+	—	—	100
Kaurenic acid*		*Sideritis* spp.	ent-kaur-16-ene-19-oic acid	+	—	—	101
Limonene	Citrus fruits	*Citrus* spp.	4-Isopropenyl-1-methyl-1-cyclohexane	—	+	+	111

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TABLE 21.1 (continued)
Natural Products from Plants that Exhibit Chemopreventive and Therapeutic Activities against Cancer

Compound	Source	Botanical Name	Structure	↓NF-κB	P	T	Ref.
Linearol*		*Sideritis* spp.		+	—	—	101
Lutein	Tomato	*Lycopersicon esculentum*		—	—	—	112,113
Lycopene	Tomato	*Lycopersicon esculentum*	ψ,ψ-Carotene	—	—	—	112–114
Oleandrin*		*Nerium oleander; Plumeria obsta*		+	—	—	115
Oxoacanthospermoldes[k]		*Milleria quinqueflora*		+	—	—	116
Parthenolide*	Feverfew	*Tanacetum parthenium and T. larvatum; Michelia champaca; Talauma ovat; Magnolia grandiflora; Artemisia myriantha*		+	—	—	117,118
Pristimerin*		*Hippocratea* spp.; *Maytenus* spp.;*Celastrus orbiculatus; Reissantia buchananii; Salacia beddomei; Heisteria pallida*		+	—	—	119
Triptolide** (PG 490)		*Tripterygium wilfordii*		+	—	—	120,121
Ursolic acid*	Basil, rosemary, berries	*Rosmarinus officinalis; Ocimum sanctum; Aronia melanocarpa; Oxycoccus quadripetalus; Origanum majorana; Diospyros melanoxylon; Salvia przewalskii Maxim*		+	—	—	122
Withanolides	Solanaceae	*Withania* spp.; *Physalis angulata; Sorpichroa origanifolia*		—	—	—	123,124

		Alkaloids					
Capsaicinoids*[l]	Pepper, red chilli, paprika fruits	*Capsicum* spp.	8-Methyl-*N*-vanillyl-trans-6-noneamide	+	+	+	125–127
Cepharanthine*		*Stephania cepharantha*		+	—	—	128
Conophylline*		*Tabernaemontana spp;, Ervatamia microphylla*		+	—	—	129
Higenamine	Ranunculaceae	*Aconitum japonicum; Argemone mexicana; Gnetum parvifolium*	Benzyl-tetrahydroisoquinoline alkaloid	—	—	—	130,131
Mahanimbine	Rutaceae	*Murraya koenigii; Clausena dunniana; Murraya siamensis*		—	+	—	132,133
Mahanine	Rutaceae	*Murraya koenigi; Micromelum minutum*		—	—	—	132
Morphine [m] and its analogs	Opium poppy	*Papaver* spp.		+	—	+	134–136
Murrayanol	Rutaceae	*Murraya koenigii*		—	—	—	133
Piperine	Black pepper	*Garcinia xanthochymus; Piper* spp.		—	—	—	115,137
Rocaglamides*		*Aglaia* spp.		+	—	—	138
Tetrandine* (sinomenine A)		*Stephania tetrandra*		+	—	—	139
Thionia diversifolia ext.		*Thtionia diversifolia*		—	—	—	140,141
		Allylthiosulfinate					
Allicin	Garlic	*Allium sativum*	2-Propene-1-sulfinothioic acid-*S*-2-propenyl ester	—	—	—	142,143
		Benz[a]phenazine					
Lapachone	Ginseng, lapacho tree, trunkwood	*Tabebuia* spp.		+	+	+	21

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TABLE 21.1 (continued)
Natural Products from Plants that Exhibit Chemopreventive and Therapeutic Activities against Cancer

Compound	Source	Botanical Name	Structure	↓NF-κB	P	T	Ref.
		Benzopyrene					
Rotenone		*Derris* spp.		+	—	—	144
		Caffeic acid phenylethyl ester					
CAPE	Honey bee propolis	*Apis mellifera capensis*		+	—	—	21
		Chlorophyll Catabolite					
Pheophorbide A		*Solanum diflorum*		+	—	—	145
		Glucosinolate					
Sulphoraphane	Brassicaceae, e.g., broccoli, cauliflower	*Brassica oleracea*	4-Methylsulphinyl butyl - isothiocyanate	—	—	—	146
		Indoles					
Indole-3-carbinol	Brassicaceae, e.g., onions, cabbage	*Allium cepa; Brassica* spp.	3-Indolemethanol	—	—	—	147
		Iridoid glycoside					
Aucubin*	Algae	*Eucommia* spp.; *Veronica* spp.; *Vitex* spp.; *Globularia* spp.		+	—	—	148
		Naptoquinone					
Plumbagin		*Plumbago zeylanica*	5-Hydroxy-2-methyl-1,4-naphtoquinone	—	—	—	149

		Phenyl Propanoid					
1′-Acetoxychavicol acetate	Zingiberaceae	*Zingiber officinale; Languas galanga*		—	—	—	28,150
		Phenolics					
Ethyl gallate	Grapes, tea, red maple	*Paeonia* spp.; *Sophora japonica; Vitis vinifera; Vitellaria paradoxa; Camellia sinensis*		+	—	—	151
Gallic acid*	Fruits, e.g., guava	*Psidium guajava; Erodium glaucophyllum; Melaleuca quinquenervia*	3,4,5-Trihydroxybenzoic acid	—	+	—	152
Gingerol	Ginger	*Zingiber officinale*	(1-[4′-Hydroxy-3′methylphenyl-]-5-hydroxy-3-decane	—	—	—	153
Morellin	Indica fruit	*Garcinia* spp.		—	—	—	154
Sphondin*		*Heracleum laciniatum;Ruta graveolens*		+	—	—	155
		Phenolic Acid					
Rosemarinic acid	Rosemary, sage	*Rosmarinus officinalis; Saliva officinalis*		—	—	—	156
Synapic acid		*Sida acuta*	4-Hydroxy-3,5-dimethoxycinnamic acid	—	—	—	157
Syringic acid		*Radix isatidis*	4-Hydroxy-3,5-dimethoxybenzoic acid	—	—	—	158,159
		Polysaccharide					
Ganoderma lucidum ext.	Reishi	*Ganoderma lucidum*		+	+	+	160

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TABLE 21.1 (continued)
Natural Products from Plants that Exhibit Chemopreventive and Therapeutic Activities against Cancer

Compound	Source	Botanical Name	Structure	↓NF-κB	P	T	Ref.
		Polyisoprenylated Benzophenone Derivatives					
Garcinol[n] and its analogs	*Garcinia indica* fruit	*Garcinia* spp.		—	—	—	161
		Phytoalexin					
Allixin	Garlic	*Allium sativum*	3-Hydroxy-5-methoxy-6-methyl-2-penthyl-4h-pyran-4-one	—	—	—	162
		Saponin					
Calagualine		*Polypodium* spp.		+	—	—	163
		Stilbene					
Resveratrol*[o] and analogs	*Japanese knotweed*; berry fruits, . E.grapes, cranberries etc.	*Polygonum cuspidatum; Veratrum* spp.; *Vitis* spp.; *Vaccinum* spp.	*trans*-3,4′,5′-Trihydroxystilbene	+	+	+	164–166
		Others					
Aged garlic ext.	Garlic	*Allium sativum*		+	—	—	167,168
α-lipoic acid*[p]	Asparagus, wheat, potatoes		1,2-Dithiolanepentanoic acid	+	—	—	169–171
Apple ext. (juice)	Apple juice	*Malus* spp.		+	—	—	172
Astaxanthin*	Microalga, algae	*Haematococcus pluvialis*	3,3′-Dihydroxy-β,β,carotene-4,4′-dione	+	—	—	173

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β-Glucan	Barley, soy bean, mushroom	*Avena sativa; Hordeum vulgare; Agaricus blazei*		—	—	—	174
β-sitosterol	Plants, nuts, lapacha tree, cactus	*Glycine max; Arachis* spp.*; Miconia rubiginosa; Opuntia ficus-indica*	α–Dihydrofucosterol	—	—	—	175
Cat's claw		*Uncaria tomentosa*		+	—	—	176
Cirsilineol	Basil, thyme	*Ocimum sanctum; Lantana montevidensis Briq.; Thymus vulgaris*		—	—	—	56
Diallylsulfide	Garlic, Chinese leek	*Allium sativum*	Diallylsulfide	—	—	—	177
Flavokawains (Kava lactones)	Kava kava	*Piper methysticum*		—	—	—	178
Germinated barley				+	—	—	179
Persenone A	Avocado	*Persea americana*	1-(Acetyloxy)-2-hydroxy-5,12,15-heneicosatrien-4-one	—	—	—	180
Pomegranate wine		*Punica granatum*		—	—	—	181
S-allylcysteine*		*Allium sativum*		+	—	—	182
Stinging nettle ext.		*Urtica dioica*		—	—	—	183
Trans-Asarone	Carrot	*Daucus carota L.*	*trans*-1-Prophenyl-2,4,5-trimethoxybenzene	—	—	—	184
Vitamin C*	Fruits and vegetables		Ascorbic acid	+	—	—	185,186
Vitamin E	Plant seeds and vegetables		α-Tocopherol	+	—	—	187,188

Note: T and P refer to therapy and prevention, respectively; the asterisk indicates that the Chemical structure is shown in Figure 21.2 (A to D).

[a] Baicalein and its derivatives include baicalin, wogonin, and wogonin, 6-methoxy-baicalein (oroxylin A).

[b] Catechins include catechin, epicatechin, epicatechingallate, epigallocatechin, and epigallocatechingallate; theaflavins are polyphenols found in fermented green tea, i.e., black tea.

[c] Synthetic compound closely related to a polyphenol isolated from the Indian plant, *Dysoxylum binectariferum*.

[d] *Glossogyne tenuifolia* is Chinese medicine Hiang-ju.

TABLE 21.1 (continued)
Natural Products from Plants that Exhibit Chemopreventive and Therapeutic Activities against Cancer

[e] Silymarin includes silybin, silibinin, silidian, and silychrist.
[f] Anethol and analogs include eugenol, bis-eugenol, isoeugenol, and anetholdithiolthione.
[g] Avicins include avicin D and avicin G.
[h] Azadirachtin analogs include axadirachtin A,B, D, H, I, etc.
[i] Curcubutacins analogs include curcubitacin B, D, E, etc.
[j] Germacranolides include 2b,5-epoxy-5,10-dihydroxy-6a-angeloyloxy-9b-isobutyloxy-germacran-8a,12-olide.
[k] Oxoacanthospermoldes include methoxymiller-9Z-enolide.
[l] Capsaicinoids include capsaicin* and analogs, e.g., resiniferatoxin* (daphnetoxin).
[m] Morphine and its analogs include KT 90 and sanguinarine.
[n] Garcinol and its analogs include isogarcinol.
[o] Resveratrol and analogs include piceatannol.
[p] α-Lipoic acid includes dihydrolipoic acid.

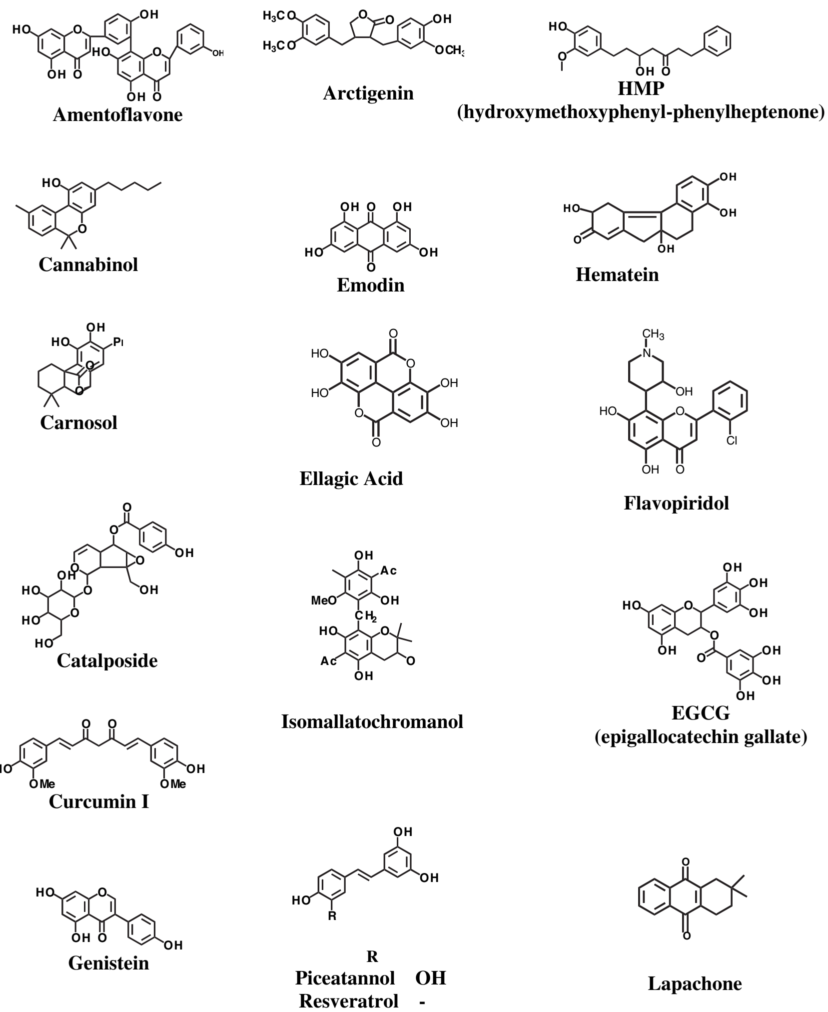
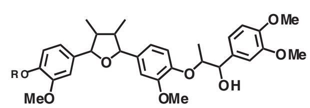
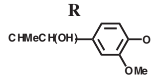
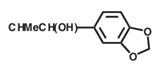
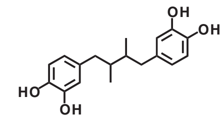


FIGURE 21.2A Structure of some plant-derived polyphenols that block NF-κB.

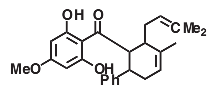
that the synergies and additive effects of such treatments, coupled with their mild nature, allow for their safe use. The increase in the popularity and awareness of complementary medicine has resulted in its use for the therapy of a variety of human diseases and by a large percentage of cancer patients. For many such patients, the use of naturally derived plant compounds and plant extracts is an essential part of their treatment. In addition, people are now more aware of the health benefits associated with the use of natural products and plant-derived compounds and have turned to these because of the negative perceptions associated with synthetic compounds. Most of the compounds outlined in Table 21.1 are commonly used in the form of concentrated plant extracts, and combinations



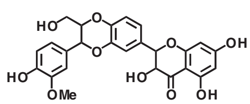
	R
Mana-ssantin A	
Mana-ssantin B	
Saucerneol	H



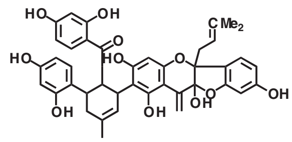
Nordihydroguaiaritic acid



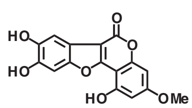
Panduratin A



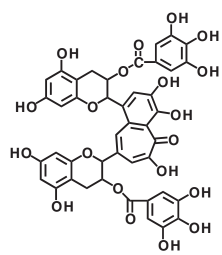
Silybin



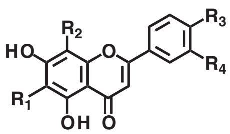
Sanggenon C



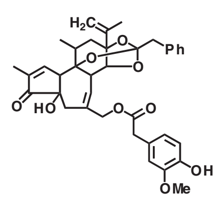
Wedelolactone



Theaflavin-3,3-digallate



	R_1	R_2	R_3	R_4
Apigenin	-	-	OH	-
Baicalein	OH	-	-	-
Luteolin	-	-	OH	OH
Oroxylin-A	OCH_3	-	-	-
Wogonin	-	OCH_3	-	-



Resinferatoxin

FIGURE 21.2B Structure of some plant-derived terpenoids that block NF-κB.

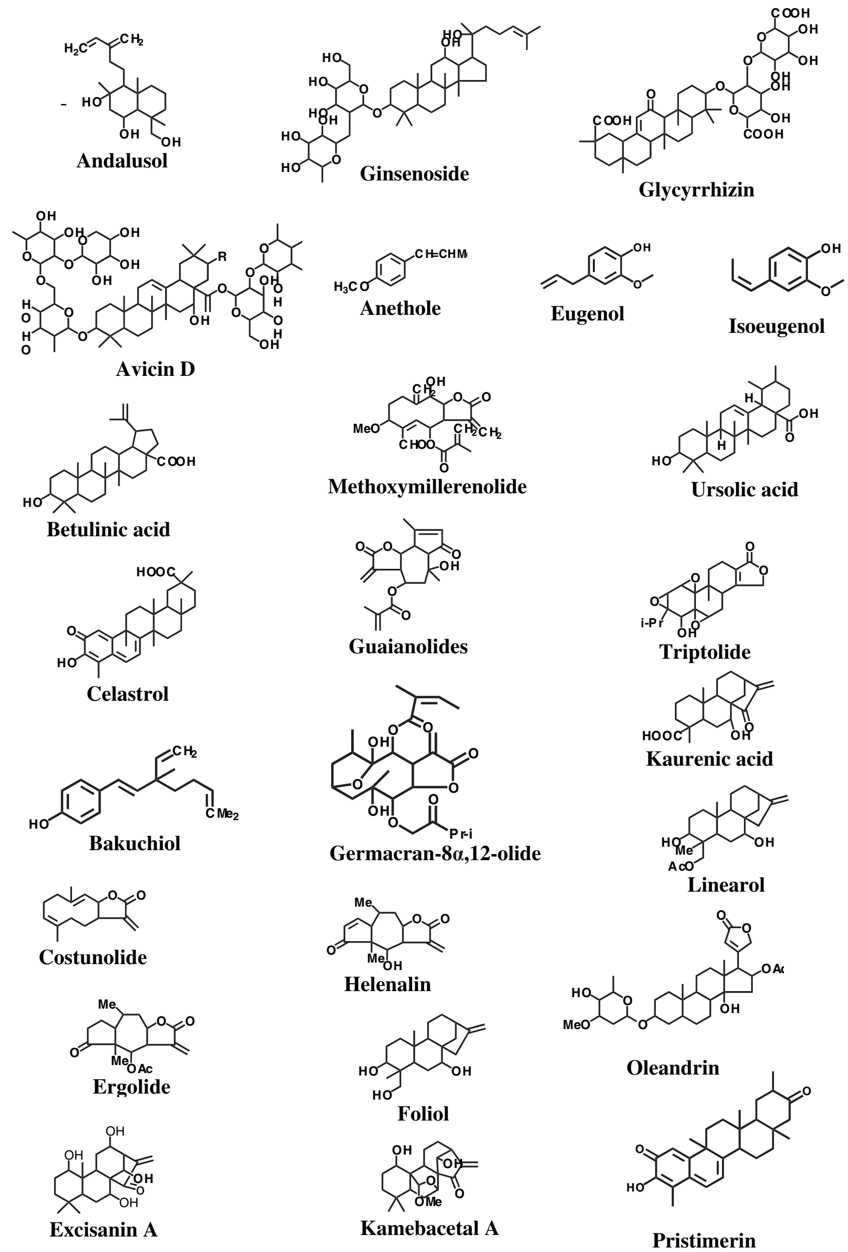


FIGURE 21.2C Structure of some plant-derived alkaloids that block NF-κB.

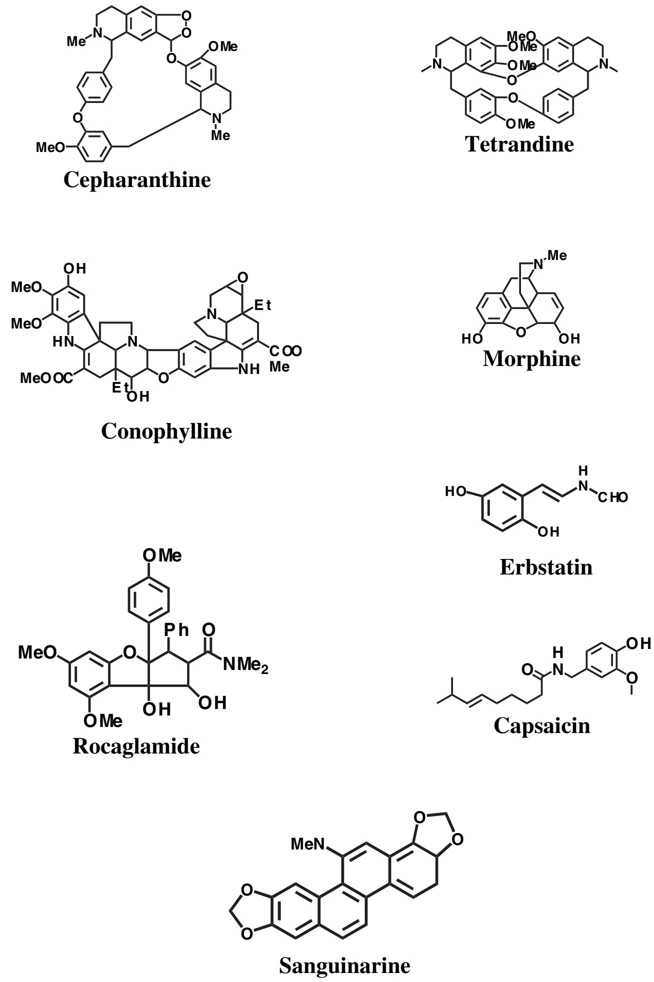


FIGURE 21.2D Structure of some plant-derived miscellaneous compounds that block NF-κB.

of these extracts can be very complex. However, although humans have been using complex mixtures for much longer than they have been using single isolated compounds or drugs, there is a need for careful standardization of dietary supplements and effective regulatory control to ensure human safety.

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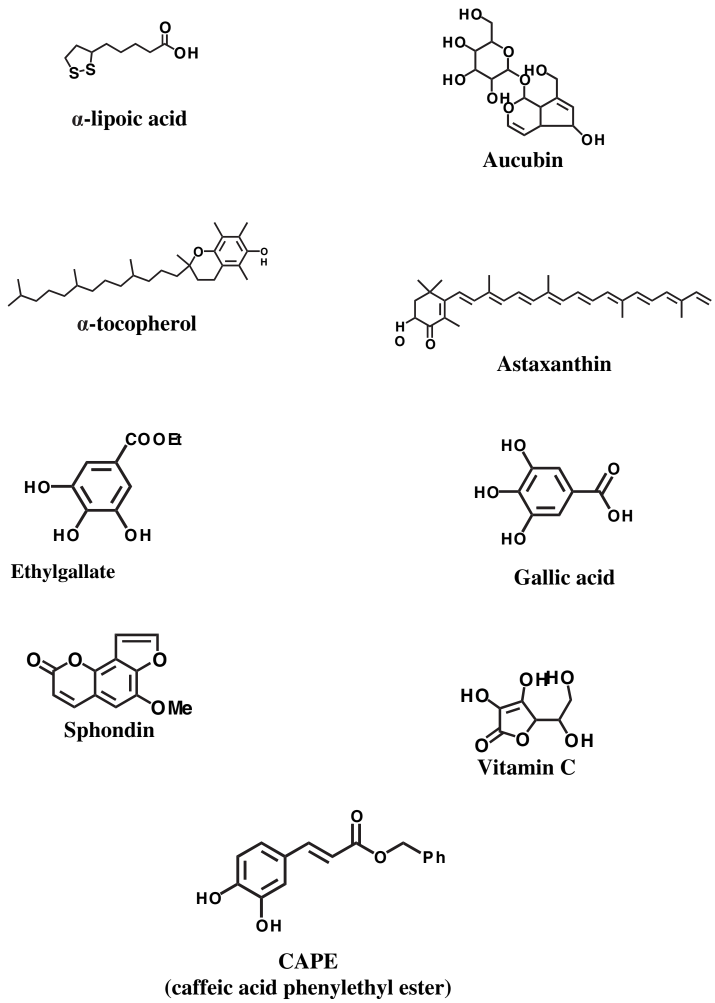

AU: Pls. provide caption for Fig. 21.2E.

FIGURE 21.2E

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ABBREVIATIONS

IκBα: inhibitory subunit of NF-κB
IKK: IκB kinase

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