

Cancer prevention and therapy with kiwifruit in Chinese folklore medicine: a study of kiwifruit extracts

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Abstract

Kiwi gold fruits were extracted successively with hexane, acetone, methanol and 70% methanol, and further fractionated by silica gel and ODS column chromatographies for the assays of various biological activities. Five fractions **H1**, **H2** (hexane extract), **A1**, **A2** (acetone extract) and **M2** (methanol extract) showed selective cytotoxic activity against human oral tumor cell lines, which was more sensitive than human gingival fibroblasts. More hydrophilic fractions [**70M3**, **70M4**, **70M5**] of 70% methanol extract displayed higher anti-HIV activity, radical generation and O₂^{•-} scavenging activity. The antibacterial activity of 70% methanol extracts [**70M0**, **70M1**, **70M2**, **70M3**, **70M4**] was generally lower than that of more lipophilic fractions (hexane, acetone, methanol extracts), although each fraction did not show any specific antimicrobial action. All fractions were inactive against *Helicobacter pylori*. These results demonstrate that gold kiwifruit extracts contain valuable, various bioactive materials, which can be separated with each other. © 2002 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: Actinidiaceae; Kiwifruit fractions; Cytotoxic activity; Antimicrobial activity; Radical intensity

1. Introduction

Kiwifruits (Actinidiaceae) is native eastern Asia where it is known as Mi-hou-tau. It is a deciduous, fruiting vine which, taxonomically, belong to the genus Actinidiaceae. In southern China kiwifruits are found growing wild in dangerous narrow glens along the river Yangtze Chang. Since ancient times people of that area have known of the very delicious flavor of kiwifruit. There has been literature on kiwifruit since the 1400's A.D. (Zhenjiang, 1980). There have been many references to cancer-like diseases in China since the oldest reference

‘nejjing’ was recorded in the 720's B.C. Hence it was recorded by ‘zhou-litian-guan’ nearly 5 centuries earlier that medicine had helped in the therapy for eight cancer patients. Their cancers were skin cancers of the hands and other cancers (Zhi, 1980). In the 7 century A.D. ‘Jin-shu’ reported Chinese traditional medicine had succeeded in treating cancer of the eye of a Chinese emperor. This treatment is the first report on the operational therapy of cancer. Later still, ‘zhu-bing-yuan-hou-lun’ (610 A.D.) or ‘san yin-fang’ (1174 A.D.) also described some cancers. In 1171 A.D., ‘wei-ji-bao-shu’ first used the description of the word ‘cancer’. In 1347 A.D. ‘Dan-xi-xin-fa’ used the word ‘lactocoele’ possibly in describing what we know of today as cancer of the mammary gland (Zhi, 1980). In ancient Chinese writings we can find many references diagnosing dis-

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eases as possible cancers. Many of these may actually be real cancers as we understand the word today. Actually, both Chinese herbal remedy and Chinese folk medicine have been used as cancer medicinals since prerecorded times (Zhi, 1980). For example, in many different cancers, especially cancer of the digestive system (mainly stomach cancer) and cancer of mammary gland, have been treated by kiwifruit prescriptions (Ai et al., 1982; Jiangsu New Medical School, 1977). These kiwifruit therapy has been used for cancer of stomach, for the treatment of lung and liver cancer of the mammary gland (Yang, 1981), for stomach cancer and rectal cancer (Ye, 1979) and for stomach cancer and rectal cancer (Zhi, 1980).

Recently, use of phytosubstances to improve or enhance their effects with safety in foods is significantly focused in daily food. The activities of diverse constituents vary in their ability by quenching effects against active free radical oxygens by carotenes and cryptoxanthins, and polyphenols and flavonoids, by inhibition of absorption into small intestine by dietary fibres, or by regulation on efflux and influx of ions in cell membranes by minerals to inhibit tumors (Motohashi et al., 1999, 2000; Shirataki et al., 2000). Therefore, the need for foods with naturally occurring substances has been strongly required.

Kiwifruit had 30–40% inhibition on sarcoma 180 of mice (Sheng, 1994). Kiwifruit juice inhibited growth of cancer cells (Song, 1984a,b). Some kiwifruit extracts showed a high 95% inhibition by Ames' test on cancer growth (Liu et al., 1994). Polysaccharides in kiwifruit inhibited growth of cancers (Li, 1996). Kiwifruits contain many medicinally useful compounds such as vitamins, carotenoids, minerals and others (Wills et al., 1986). Kiwifruit extract inhibited the growth of cultured human hepatoma cell (BEL-7404) (Jin-long et al., 1985), Ehrlich ascites carcinoma and HeLa cells (Kosuge et al., 1985), and reduced the nitrosation reactions (which is important in cancer induction) by efficiently nitrile scavenging activity of ascorbic acid present in extracts (Normington et al., 1986).

In contrast, no detailed study of the biological activity of kiwifruit gold fruits extract has been reported so far. This urged us to investigate biological activity of kiwifruit gold fruit extract, using a new kiwifruit of Hort 16 (Gold) originally selected by seedlings in 1991 (The Horticulture and Food Research Institute of New Zealand, 1999).

2. Materials and methods

2.1. Materials

New kiwifruits of Hort 16 (Gold) were supplied by New Zealand Kiwifruit Marketing Board (ZESPRI)

(The Horticulture and Food Research Institute of New Zealand, 1999). This is also cultivated in the laboratory farm attached to Josai University (Address: 1-1 Keyakidai, Sakado, Saitama 350-0290, Japan; Tel./fax: +81-49-271-7053) and a voucher specimen (Hort 16) is deposited in the Herbarium of Josai University.

2.2. Compounds and nutrient media

The following chemicals and reagents were obtained from the indicated companies: RPMI1640 medium, Dulbecco's modified Eagle medium (DMEM) (Gibco BRL, Grand Island, NY); fetal bovine serum (FBS) (JRH Biosci, Lenexa, KS); 3-(4,5 dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) (Wako Pure Chem. Ind., Ltd, Osaka); Gallic acid (G0011, Tokyo) and alkali-lignin (L-0082, Tokyo) were purchased from Tokyo Kasei Organic Chemicals, Tokyo. (–)-Epigallocatechin gallate (EGCG) (059-05411) was purchased from Wako Chemicals, Tokyo. 3'-azido-2',3'-dideoxythymidine (AZT), dideoxycytidine (ddC) (Sigma Chem. Co., St. Louis, MO); dextran sulfate (8 kD) (Kowa, Tokyo); curdlan sulfate (300 kD) (Ajinomoto, Tokyo); diethylenetriaminepentaacetic acid (DETA-PAC) (Sigma); 3,4-dihydro-2,2 dimethyl-2H-pyrrole-1-oxide (DMPO) (a spin trap agent) (Aldrich Chemical Comp. Inc., USA); superoxide dismutase (SOD) from bovine erythrocytes (Dojin, Kumamoto, Japan). Human red blood cells were collected from the heparinized peripheral blood of normal donors.

2.3. Bacterial strains and eucaryotic cell lines

A strain of *Helicobacter pylori* (ATCC43504) was purchased from American Type Culture Collection (Rockville, MD). *Staphylococcus epidermidis* ATCC 12228, *Pseudomonas aeruginosa* 27853, *Escherichia coli* K12LE140 and *Candida glabrata* clinical isolates were obtained from Central Laboratory of clinical Microbiology, Szeged University.

2.4. Preparation of kiwifruit extracts

Dried kiwifruits of Hort 16 (Gold) (365 g), supplied by ZESPRI of New Zealand, were successively extracted with hexane, acetone, MeOH and 70% MeOH at room temperature and the solvent was concentrated *in vacuo*, and the hexane extract [H0] (0.15 g), acetone extract [A0] (11.2 g), MeOH extract [M0] (267.1 g) and 70% MeOH extract [70M0] (25.3 g) were obtained, respectively.

First, the aliquot of hexane extract [H0] (0.14 g) was applied to a silica gel column chromatography, which was then eluted with a hexane–acetone gradient. The hexane fraction and hexane–acetone (9:1) fraction [H1] (0.023 g), hexane–acetone (4:1) fraction and hexane–acetone (1:1) fraction [H2] (0.028 g) were stepwisely

eluted. Second, the acetone extract [A0] (10 g) was applied to a silica gel column chromatography, which was then eluted with a benzene–EtOAc gradient. The benzene fraction and benzene–EtOAc (9:1) fraction [A1] (0.25 g), benzene–EtOAc (4:1) fraction [A2] (0.05 g), benzene–EtOAc (3:2) fraction [A3] (0.25 g) and benzene–EtOAc (1:1) fraction [A4] (0.13 g) were stepwisely eluted. Third, the MeOH extract [M0] (20 g) was applied to a silica gel column chromatography, which was then eluted with a CHCl₃–MeOH gradient. The CHCl₃ fraction [M1] (0.15 g), CHCl₃–MeOH (49:1) fraction [M2] (0.07 g), CHCl₃–MeOH (24:1) fraction [M3] (0.12 g), CHCl₃–MeOH (9:1) fraction [M4] (1.80 g) and CHCl₃–MeOH (4:1) fraction [M5] (12.30 g) were stepwisely eluted. Finally, the 70% MeOH extract [70M0] (20 g) was applied to an ODS column chromatography, which was then eluted with a H₂O–MeOH gradient. The H₂O–MeOH (2:1) fractions [70M1] (0.28 g), [70M2] (18.09 g), [70M3] (0.27 g), H₂O–MeOH (1:1) fraction [70M4] (0.053 g) and [70M5] (0.026 g) were stepwisely eluted (Fig. 1).

2.5. Assay for cytotoxic activity

Human squamous cell carcinoma (HSC-2) and human oral gingival fibroblasts (HGF) (5–7 population doubling levels) were cultured in DMEM medium supplemented with 10% heat-inactivated FBS. These cells were incubated for 24 h with the indicated concentrations of test samples. The relative viable cell number (absorbance at 540 nm (A_{540})) was then determined by MTT assay. The 50% cytotoxic concentration (CC_{50}) was determined from the dose–response curve (Table 1).

2.6. Assay for anti-human immunodeficiency virus activity (Nakashima et al., 1992)

Human T cell leukemia virus 1 (HTLV1)-bearing CD4 positive human T cell lines, MT-4 cells, were infected with HIV-1_{IIIB} at a multiplicity of infection (m.o.i.) of 0.01. HIV- or mock-infected MT-4 cells (1.5×10^5 /ml, 200 μ l) were placed into 96-well microtiter plates and incubated in the presence of varying concentrations of the fractions. After incubation for 5 days at 37 °C in a 5% CO₂ incubator, cell viability was quantified by a colorimetric assay (at 540 nm and 690 nm), monitoring the ability of viable cells to reduce MTT to a blue formazan product (Nakashima et al., 1992). All data represent the mean values of triplicate measurements. CC_{50} was determined with mock-infected cells, whereas EC_{50} was determined with HIV-infected cells. Selectivity index (SI) was defined as follows:

$$SI = CC_{50}/EC_{50}.$$

2.7. Antimicrobial activity

Each 10 mg fraction was dissolved in 1 ml DMSO, and stock solution 25 μ l was placed into a filter paper disk (250 μ g/disk) and the disk was placed to the minimal tryptone-yeast (MTY) (Alföldi et al., 1968) agar and blood agar surface inoculated with 10^5 cells of the indicated strains. After 24 h incubation, the diameters of inhibiting zones were measured in mm. As a control, 25 μ l DMSO was applied by the same method. The *Candida albicans* and *Candida glabrata* strains grew on 2 $\times$ YPD (van der Walt and Yarrow, 1984) and MTY extract nutrient agar.

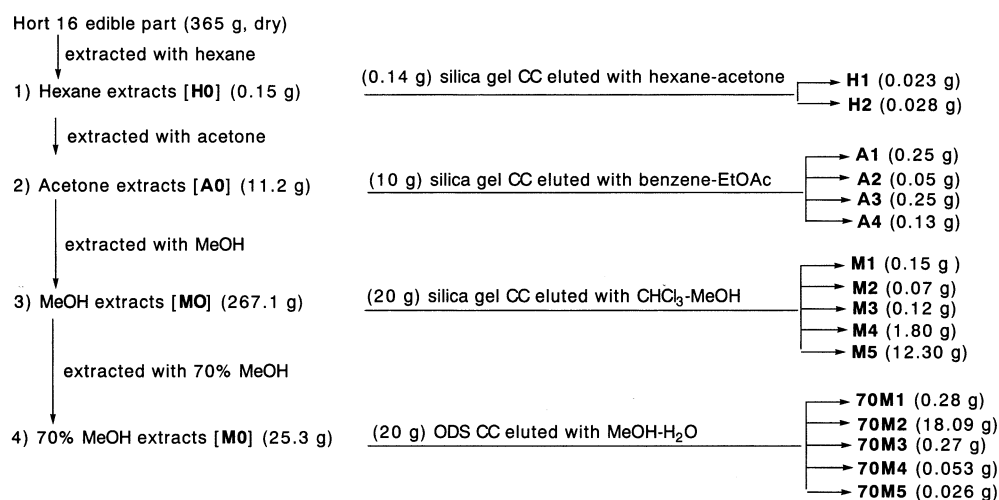


Fig. 1. Fractional separation of kiwifruit extracts. CC, column chromatography.

Table 1
Diverse biological activity of kiwifruit extracts

Extract or fraction	Cytotoxic activity ^a (CC ₅₀ :µg/ml)			Anti-HIV activity			Radical generation				O ₂ [−] scavenging activity (SOD unit/mg)
	Human oral tumor cell line		Human gingival fibroblast (HGF)	CC ₅₀ (µg/ml)	EC ₅₀ (µg/ml)	SI (CC ₅₀ /EC ₅₀)	pH8	pH 9	pH 10.5	pH 12.5	
	HSC-2	HSG									
H0	429	568	888	133	> 200	< 1	< 0.04	< 0.04	< 0.04	< 0.04	0.31
H1	218	360	420	42	> 200	< 1	< 0.04	< 0.04	< 0.04	< 0.04	0.21
H2	220	363	815	108	> 200	< 1	< 0.04	< 0.04	< 0.04	< 0.04	0.44
A0	> 1000	> 1000	> 1000	> 200	> 200	> < 1	< 0.04	< 0.04	< 0.04	< 0.04	3.89
A1	193	291	426	124	> 200	< 1	< 0.04	< 0.04	< 0.04	< 0.04	0.29
A2	239	354	728	113	> 200	< 1	< 0.04	< 0.04	< 0.04	< 0.04	0.36
A3	680	705	993	131	> 200	< 1	< 0.04	< 0.04	1.71	0.25	21.60
A4	753	861	> 1000	> 200	> 200	> < 1	< 0.04	< 0.04	0.31	0.13	3.75
M0	> 1000	> 1000	> 1000	> 200	> 200	> < 1	< 0.04	< 0.04	< 0.04	< 0.04	2.73
M1	818	982	> 1000	> 200	> 200	> < 1	< 0.04	< 0.04	< 0.04	< 0.04	0.40
M2	173	185	414	73	> 200	< 1	< 0.04	< 0.04	< 0.04	< 0.04	0.47
M3	324	424	928	91	> 200	< 1	< 0.04	< 0.04	< 0.04	0.09	1.73
M4	965	> 1000	> 1000	> 200	> 200	> < 1	< 0.04	< 0.04	< 0.04	< 0.04	12.84
M5	950	> 1000	> 1000	> 200	> 200	> < 1	< 0.04	< 0.04	< 0.04	< 0.04	1.19
70M0	845	> 1000	> 1000	> 200	> 200	> < 1	< 0.04	< 0.04	< 0.04	< 0.04	3.55
70M1	> 1000	> 1000	> 1000	> 200	> 200	> < 1	< 0.04	0.08	0.10	0.22	8.01
70M2	920	> 1000	> 1000	> 200	> 200	> < 1	< 0.04	< 0.04	0.07	0.11	5.21
70M3	958	843	> 1000	> 200	18.5	> 11	< 0.04	0.28	0.26	0.48	16.28
70M4	> 1000	995	> 1000	> 200	7.6	> 26	0.09	0.25	0.20	0.70	9.85
70M5	> 1000	885	> 1000	> 200	14.1	> 14	< 0.04	0.20	0.22	0.64	7.89
Gallic acid	77	80	90				0.20	0.85	0.70(1.60 mM)		571.00
EGOG	137	141	ND ^b						2.43(0.60 mM)		
Alkali–lignin											7.10
Dextran sulfate				518	0.40	1295					
Curdean sulfate				> 1000	0.20	> 5000					
AZT(µM)				267	0.014	19 071					
ddc(µM)				1690	0.74	2283					

^a Near confluent HSC-2, HSG and HGF cells were incubated for 24 h with various concentrations of kiwifruit extracts, and the relative viable cell number (A₅₄₀) was determined by MTT method. Each value represents mean from duplicate determinations. Control A₅₄₀ values of HSC-2, HSG and HGF cells were 1.138, 0.804 and 0.507, respectively.

^b ND, not determined.

2.8. Anti-*H. pylori* activity

Mueller–Hilton broth containing 5% FBS was used as the medium, and was cultured in a jar conditioned with Campylo Pack (Dia latron) for 48 h. Briefly, *H. pylori* strains were inoculated on a Brucella agar plate containing 10% horse serum, and cultured at 37 °C for 48 h. The bacterial colonies collected were diluted to 10⁷ colony forming unit (CFU)/ml with 0.9% saline. The extracts were dissolved in DMSO, and then diluted with Mueller–Hilton broth. To the solution of the extracts, each bacterial suspension was added to a density of 10⁶ CFU/100 ml/well. The mixture was incubated at 37 °C for 48 h. The minimum inhibitory concentration (MIC) of each fraction was calculated from the dose–response curve (Numao et al., 1997; Kawase et al., 1999).

2.9. Assay for radical intensity

Radical intensity was determined at 25 °C using ESR spectroscopy (JEOL JES RE1X, X-band, 100 kHz modulation frequency). Instrument settings: center field, 335.6±5.0 mT; microwave power, 8 mW; modulation amplitude, 0.1 mT; gain, 630; time constant, 0.03 s; scanning time, 2 min. Radical intensity was determined in 0.1 M Tris–HCl buffer (pH 8.0), 0.1 M NaHCO₃/Na₂CO₃ buffer (pH 9.0 or 10.5) or 0.1 N KOH (pH 12.5) containing 50% DMSO, and the radical intensity was defined as the ratio of peak heights of these radicals to that of MnO (Satoh et al., 1997).

2.10. Superoxide anion (O₂[−]) scavenging activity

O₂[−] was generated by hypoxanthine (HX) and xanthine oxidase (XOD) reaction (200 µl) (2 mM (in PBS) HX 50 µl, 0.5 mM DETAPAC 20 µl, DMPO 10 µl, sample (in DMSO) 50 µl, H₂O or SOD 30 µl, XOD (0.5 U/ml of 0.1 M PBS, pH 7.8) 40 µl). The time constant and scanning time was changed to 0.03 s and 2 min, respectively. O₂[−] scavenging activity was expressed as SOD unit/mg sample.

3. Results

3.1. Cytotoxic activity

Cytotoxic activity was increased with the decrease in the water-solubility: hexane extract > acetone extract > methanol extract > 70% methanol extract (Table 1). Five fractions **H1**, **H2** (hexane extract), **A1**, **A2** (acetone extract) and **M2** (methanol extract) showed selective cytotoxic activity against human oral tumor cell lines (HSC-2, HSG), than against HGF (Table 1). Cytotoxic activity of these fractions (CC₅₀ = 173–239 µg/ml) was

slightly lower than that of gallic acid (CC₅₀ = 77 µg/ml) and EGCG (CC₅₀ = 137 µg/ml) (Table 1).

3.2. Anti-human immunodeficiency virus activity

Anti-HIV activity (SI = 11–26) was detected only in 70% methanol fractions (**70M3**, **70M4**, **70M5**), and their anti-HIV activity was much lower than that of dextran sulfate (SI = 1295), curdlan sulfate (SI > 5000), AZT (SI = 19071) and ddC (SI = 2283) (Table 1). Other fractions were inactive (SI = 1) (Table 1).

3.3. Antimicrobial activity

Antibacterial activity of 18 fractions of extracts against Gram-positive *Staphylococcus epidermidis* ATCC 1228, Gram-negative *Pseudomonas aeruginosa* 27853, and *E. coli* K12 LE140, and fungus (*Candida albicans*, *Candida glabrata*) was investigated (Table 2). **H1**, **M2** and **M3** were effective to *Staphylococcus epidermidis* ATCC 1228. **H1**, **A1**, **A3**, **A4**, **M3** and **70M5** were effective to *Pseudomonas aeruginosa* 27853. **A2** alone was the most effective to *E. coli* K12 LE140, whereas all six fractions of 70% methanol extract were inactive to *E. coli*. All fractions were effective to *Candida glabrata* (cultivated on MTY agar) (Table 2). Generally, the antimicrobial activity of 70% methanol extracts [**70M0**, **70M1**, **70M2**, **70M3**, **70M4**] was lower than that of more lipophilic fractions (hexane, acetone or methanol extracts) (Table 2). All these fractions did not show any specific antimicrobial action.

All 26 fractions (MIC₅₀ ≥ 100 µg/ml) were inactive against *H. pylori*, in contrast to metronidazole (MIC₅₀ = 74.0 µg/ml), clarithromycin (MIC₅₀ = 1.9 µg/ml), or erythromycin (MIC₅₀ = 1.8 µg/ml) (Table 2).

3.4. Radical generation

Generally, water-soluble fractions produce higher amounts of radical under alkaline conditions, except two acetone extract fractions [**A3**, **A4**] producing transient multipeak radicals at pH 10.5 (Fig. 2). On the other hand, 70% methanol extract fractions [**70M1**, **70M2**, **70M3**, **70M4**, **70M5**] produce broad peak of radical at pH 9.0–12.5 (Fig. 2, Table 1). We have previously reported similar broad peak of alkali-lignin under alkaline condition (Satoh et al., 1996). The radical intensity of these fractions were comparable with that of gallic acid (0.70 at 1.6 mM) and EGCG (2.43 at 0.6 mM) (Table 1).

3.5. Relationship between radical intensity and O₂[−] scavenging activity

Generally, the fractions which produce radicals [**A3**, **A4**, **70M1**, **70M2**, **70M3**, **70M4**, **70M5**] scavenge O₂[−]

Table 2
Antimicrobial activity of kiwifruits extracts^a

Extract or fraction	Gram-positive	Gram-negative		Fungi (<i>Candida</i>)	<i>Helicobacter pylori</i>
	<i>Staphylococcus epidermidis</i> ATCC 12228	<i>Pseudomonas aeruginosa</i> 27853	<i>Escherichia coli</i> K12LE140	<i>Candida glabrata</i> (cultivated on MTY agar)	MIC ₅₀ (μg/ml) ^b
H0	+	+	+	++	ND ^c
H1	++	++	+	++	> 100
H2	+	+	–	++	> 100
A0	–	+	–	++	ND
A1	+	++	+	++	> 100
A2	+	+	++	++	> 100
A3	+	++	–	++	> 100
A4	+	++	–	++	> 100
M0	+	–	+	++	ND
M1	+	+	+	+	> 100
M2	++	–	+	++	> 100
M3	++	++	+	++	> 100
M4	–	+	–	++	> 100
M5	–	+	–	+	> 100
70M0	–	+	–	+	ND
70M1	+	+	–	+	> 100
70M2	+	+	–	+	> 100
70M3	+	+	–	+	> 100
70M4	+	+	–	+	> 100
70M5	+	++	–	+	> 100
Gentamicin (20 μg)	++	++	++	ND	
Amphotericin B (20 μg)	ND	ND	ND	++	
Gallic acid (20 μg)	–	–	–	–	
Metronidazole					74.0
Clarithromycin					1.9
Erythromycin					1.8

^a For bacteria: +, inhibitory zones varied from 7 mm to 10 mm; ++, inhibitory zones varied from 11 mm to 12 mm. For fungi: +, inhibitory zones varied from 0.5 mm to 2 mm; ++, inhibitory zones varied from 2.5 mm to 4.5 mm. One Gram-positive (1) and two Gram-negative (2, 3) strains were not sensitive to DMSO. One fungi (4) was sensitive to DMSO.

^b The MIC value was determined for each compound by a broth microdilution method using *H. pylori* (ATCC43504) by the following literatures (Kawase et al., 1999; Numao et al., 1997).

^c ND, not detected.

(produced by HX–XOD reaction) more efficiently than those which do not produce radical (Fig. 3, Table 1). There are only two exceptions: **A3** and **M4**. The SOD activity of these fractions were between that of gallic acid (571 SOD unit/mg) and alkali-lignin (7.1 SOD unit/mg) (Table 1).

4. Discussion

Various hydrophobic fractions of gold kiwifruit extract exerted different biological activities against prokaryotic and eukaryotic cells and some virus species including HIV. As media methods for expression of multidrug reversal action, there is a binding formation between kiwifruit extracts and specific cell membrane components such as two isoforms of an apical Na⁺

channel or one single type of channel with two type's covalent binding sites of both higher and lower affinities (Barbry et al., 1989), or a peptide of α -tubulin bind to a taxoid binding site (Loeb et al., 1997). However, the mechanism of action of the biological effect can be also explained by special radical generation or scavenging some type of free radicals. Activity of extracts was increased with the decrease in the water and three 70% methanol extracts [**70M3**, **70M4**, **70M5**] showed the highest anti-HIV activity, produced broad radical under alkaline condition, and scavenged the O₂[–] radical. Their properties were similar to lignin, which showed comparable anti-HIV activity, and produced similar ESR pattern of radical generation and O₂[–] scavenging activity (Sakagami et al., 1999). Interestingly, the radical generation (assayed at an alkaline pH) roughly paralleled O₂[–] scavenging activity (assayed at a neutral pH).

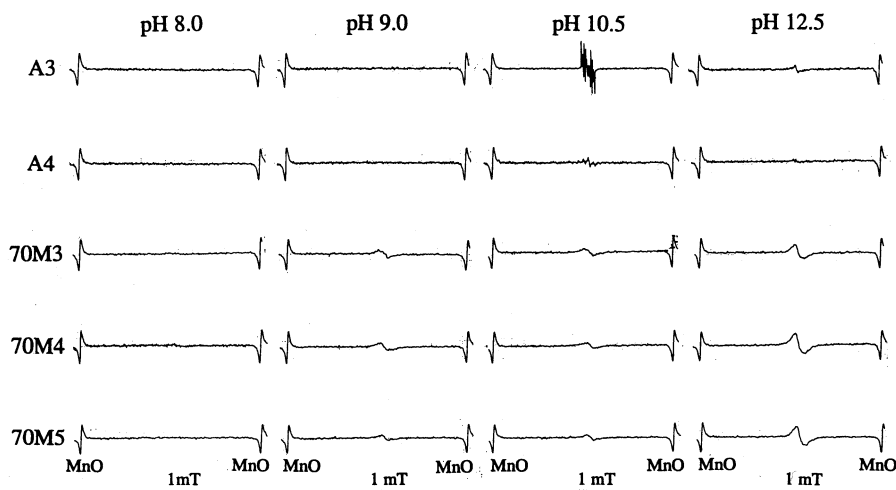


Fig. 2. ESR spectra of kiwifruit extracts. ESR spectra were measured 1 min after dissolving sample in 0.1 M Tris–HCl buffer (pH 8.0), 0.1 M NaHCO₃/Na₂CO₃ buffer (pH 9.0 or 10.5), or 0.1 N KOH (pH 12.5) containing 50% DMSO. The amplitude and gain were changed to 0.1 mT and 1×1000 , respectively.

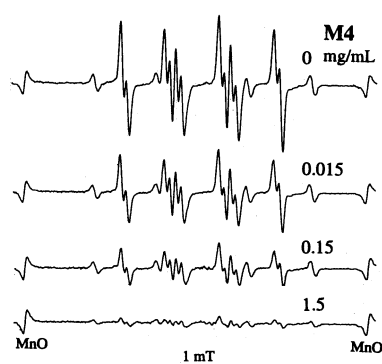


Fig. 3. O₂^{•−} scavenging activity of M4.

This supports that many of the extracts show both prooxidant (at higher concentration) and antioxidant actions (at lower concentration). There remains to investigate how the same molecule switches from prooxidant action to antioxidant action, and vice versa. The kiwifruit gold extracts has also tumor selective, cytotoxic activity and antimicrobial activity, which can be distinct from anti-HIV activity. These results indicate that kiwi gold fruits extracts contain therapeutically useful substances. Further purification of these fractions is required to confirm this point.

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