“Raffinee,” a Free Radical Scavenger, in the Treatment of Subacute Stage Brain and Spinal Cord Lesions: A Case Report

Hsin-Ying Chen¹, Jer-Min Lin² and Chun-Ching Lin³*

¹Graduate School of Medicine, Kaohsiung Medical College, Kaohsiung, Taiwan
²Ziel Enterprise, Kaohsiung, Taiwan
³School of Pharmacy, Kaohsiung Medical College, Kaohsiung, Taiwan
* Corresponding author

(Accepted for publication May 23, 1997)

Abstract: This report presents the effects of the natural antioxidant formulation “Raffinee” in treatment of a case with subacute cerebellar hemorrhage and a case with subacute incomplete cervical cord injury. Four days after onset of cerebellar hemorrhage, the regimen started and ameliorated severe headache and dizziness within 3 days. Forty-five days after incomplete spinal cord injury with marked edema of cervical cord, the regimen started. Excellent motor and sensory function recovery were obtained within one month with remission of cord edema. The dosage of “Raffinee” is equivalent to 2,280,000 units of superoxide radical scavenging activity and 47,000 units of hydroxyl radical scavenging activity. Based on the secondary injury theory, superoxide and hydroxyl radical scavengers may have a valuable use in subacute central nervous system (CNS) lesions. Further larger scale of randomized, placebo-controlled, double-blind clinical trials are indicated to verify the effect of “Raffinee” on subacute CNS lesions.

Focal central nervous system (CNS) primary injuries such as infarctional stroke, hemorrhagic stroke, head injury, aneurysmal rupture, and spinal cord injury, inevitably result in death of neurons in the damaged area. There remains an adjacent zone of surviving neurons and glial tissues prone to further injury. In the case of cerebral infarction, the cascade of injurious events begins within minutes of ischemia, and permanent neuronal injury may occur in the center of the ischemic area within 6-8 minutes (Scheinberg, 1994). However, a variable window of therapeutic opportunity probably continues for several hours or days after injury, at least with respect to peripheral portions of the ischemic zone. In the case of spinal cord injury, primary injury usually is derived from acute compression or laceration of
the spinal cord due to displacement of bone or disc into the spinal cord during fracture-dislocation or bursting fracture of the spine (Tator, 1983). However, mechanical injury rarely transects the cord completely, even when the injury is neurologically complete (Kakukas, 1984). In addition, biochemical and pathological changes in the spinal cord may worsen after injury. To explain these phenomena, the concept of secondary injury has evolved for which numerous pathophysiological mechanisms have been postulated (Tator and Fehlings, 1991; Siesjo, 1992; Petty et al., 1996). There are major changes in the secondarily injured CNS tissues:

1. Reduction of microcirculation due to vasospasm and platelet aggregation (Nelson et al., 1977), and loss of autoregulation (Guha et al., 1989).
2. Increased intracellular calcium and sodium ions following activation of NMDA (N-methyl-D-aspartate) receptor by a large amount of glutamate released from damaged neurons (Faden and Simon, 1988).
3. Free radical formation and lipid peroxidation of cell membrane (Gutteridge, 1995).

According to the secondary injury theory, several neuroprotective agents have proved to be effective experimentally, but only the agents with antioxidant and free radical scavenging effects succeeded in clinical studies (Bracken et al., 1990; Asano et al., 1996). Therefore in this study, we treated subacute brain and spinal cord lesions with a natural antioxidant formulation “Raffinee.”

Materials and Methods

“Raffinee” is a brand of liquid form SOD-like natural antioxidant formulation. This product was developed by Ziel enterprise in Taiwan and Toyo Hakko company in Japan. The main component of “Raffinee” is GMT (Germ extract), which is made by fermentation and infrared treatment of extracts of rice germ and soy bean. GMT contains flavonoids, amino acids, nucleic acids, vitamins, and minerals (Table 1). The flavonoids, including (+)-epigallocatechin gallate, (−)-epigallocatechin, (−)-epicatechin and D-(−)-catechin, are potent antioxidants with very low molecular weight (300-500) (Figure 1) (Okuda et al., 1983; Uchida et al., 1987; Hatao et al., 1989). The composition of “Raffinee” is shown in Table 2. Each portion of “Raffinee” contains 10 ml of transparent brown color liquid filled by aseptic vacuum technique in a plastic cup covered by a special sheet. This highly technological filling method guarantees preservation of the product for 2 years without preservatives.

The free radicals scavenging activities of “Raffinee” were evaluated by Dr. Lin with ESR spectrometry in Japan. The procedures, chemicals, and equipment of ESR spectrometry are listed below.

Chemicals

Spin trapping reagent: 5,5-Dimethyl-pyrroline-N-oxide (DMPO) was purchased from Labotec, Tokyo, Japan. Trace metal impurities present in the chelating agent: diethylene-triamine-pentaacetic acid (DETPAC) and hypoxanthine (HPX) were from Sigma Chemical. Xanthine oxidase (XOD) and superoxide dismutase, (SOD) were obtained from
Clinical Use of Raffinee in CNS Lesions

Boehringer Mannheim and Toyobo, Osaka, respectively, L(+)-Ascorbic acid, ferrous sulfate and hydrogen peroxide were purchased from Wako Pure Chemical. Sodium phosphate buffer solution (PBS) (pH 7.8) from Taiwan was of analytical grade.

Table 1. Chemical Analysis of GMT (Rice Germ and Soybean Extract)

1. Flavonols
   - (-)-epigallocatechin gallate
   - (-)-epigallocatechin
   - (-)-epicatechin
   - D(-)-catechin
2. Nucleic acids
   - Adenine, guanine, cytosine, thymine, uracil
3. Amino acids
   - Asparagine, threonine, serine, glutamic acid, proline, glycine, alanine, cystine, valine, methionine, isoleucine, tyrosine, phenylalanine, histidine, lysine, tryptophan, arginine
4. Vitamins
   - Thiamine, riboflavin and niacin
5. Minerals
   - Calcium, phosphorus, iron, sodium, potassium
6. Other compound
   - Phytic acid, caffeine

Data source: Japan Food Analysis Center

Figure 1. Chemical structure and molecular weight of flavonols.
Table 2. Composition of Raffinee

<table>
<thead>
<tr>
<th>Component</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GMT (rice germ. soybean extract)</td>
<td>80%</td>
</tr>
<tr>
<td>Oligosaccharide</td>
<td>14%</td>
</tr>
<tr>
<td>DL-Alanine</td>
<td>2.5%</td>
</tr>
<tr>
<td>Green tea extract</td>
<td>1.2%</td>
</tr>
<tr>
<td>Dietary fiber (Pine apple fiber)</td>
<td>1.0%</td>
</tr>
<tr>
<td>Citric acid</td>
<td>0.6%</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>0.5%</td>
</tr>
<tr>
<td>Calorie</td>
<td>4.2 Kcal/portion</td>
</tr>
<tr>
<td>Superoxide radical scavenging activity</td>
<td>380,000 SOD unit/portion</td>
</tr>
<tr>
<td>Hydroxyl radical scavenging activity</td>
<td>7,900 AsA unit/portion</td>
</tr>
</tbody>
</table>

SOD: Superoxide dismutase, AsA: Ascorbic acid. Data source: Japan Food Analysis Center

Superoxide Radicals Generating System (McCord & Fridovich, 1969; Mitsuta et al., 1990)

Superoxide radicals were generated from a hypoxanthine-xanthine oxidase reaction system, trapped by DMPO, and the spin adduct DMPO-OH was analyzed using an ESR spectrometer. The procedure was as follows: a solution of 2.0 mM HPX/PBS (a), 5.5 mM DETAPAC/PBS (b), various concentrations of SOD or Raffinee (c), and 0.4 units/ml XOD/PBS (d) were prepared before use. The XOD solution was stored in an ice bath to prevent any activation of enzyme. Fifty microliters of (a), 35 μl of (b), 50 μl of (c), and 15 μl DMPO (9.2 M) were put into a test tube. To the mixed solution, 50 μl of (d) was added.

Hydroxyl Radicals Generating System: (Kohno et al., 1991)

Hydroxyl radicals were generated from the following procedure: A solution of 1 mM ferrous sulfate (a), 5.5 mM DETAPAC/PBS (b), various concentrations of ascorbic acid or Raffinee (c), and 1 mM hydrogen peroxide (d) were prepared before use. 37.5 μl of (a), 37.5 μl of (b), 50 μl of (c), and 20 μl DMPO (0.092 M) were put into a test tube, then 75 μl of (d) was added to the mixed solution. Analysis of the spin adduct DMPO-OH was performed with an ESR spectrometer.

ESR Spectrometry

The reaction mixture was stirred and transferred to a quartz analyzing cell and placed into the cavity of the ESR spectrometer (JEOL-JES-80 FR, JEOL, Tokyo, Japan). Forty seconds after the addition of XOD or hydrogen peroxide, samples were analyzed and the relative intensity of the signal of DMPO-OH or DMPO-OH spin adduct was measured as the ratio to the intensity of Mn$^{2+}$ signal. ESR spectra were recorded at 37°C with a field set 335.4 ± 5.0 mT, modulation frequency 100 kHz, modulation amplitude 0.79 x 0.1 mT, response time 0.1 second, sweep time 2 minutes, microwave power 8.0 mW (9.416 GHz), receiver gain 2 x 100 when superoxide radicals were trapped, and 1 x 100 when hydroxyl radicals were trapped.
a. Reactivity to Superoxide Radical

When DMPO was added to a solution of the HPX-XOD reaction system, the spin adduct DMPO-OOH was formed (Figure 2). When SOD of various concentrations was added to the system, the signal intensities of DMPO-OOH decreased with an increase in the SOD concentration, and the inhibition ratio using the standard SOD was calculated. The linear calibration curve using a standard SOD (0.18.66 unit/ml) solution was determined with peak intensities of the internal standard signal in MnO, which was set in the ESR spectrometer and the superoxide radical.

![Figure 2. ESR signals of superoxide radical from DMPO-OOH adduct without SOD. Mn²⁺ signal as a standard.](image)

A phenomenon similar to the addition of SOD occurred with the addition of Raffinee. The scavenger activity of Raffinee was obtained from the calibration curve by comparing the averaged relative peak height of Raffinee and that of standard SOD (SOD-like activity). 0.11 milligrams per milliliter of Raffinee caused approximately the same effect as 5.194 unit/ml of SOD (IC₅₀) with respect to inhibiting averaged relative peak height by 50%. This result means that the superoxide radical scavenging activity of Raffinee is 38,000 units per gram, 380,000 units per potion (10 ml) (Table 3).

b. Reactivity to Hydroxyl Radical

The spin adduct DMPO-OH was formed when DMPO was added to a solution of the ferrous sulfate-hydrogen peroxide reaction system (Figure 3).

Ascorbic acid, used as a scavenger of hydroxyl radicals, was added to the reaction system. Then the signal decayed with increasing ascorbic acid concentration (0 1.0 mM).
The calibration curve was determined with peak intensities of the internal standard signal of Mn$^{2+}$ in MnO and the hydroxyl radical.

Table 3. SOD Activity Assay, Standard Data and Raffinee

<table>
<thead>
<tr>
<th>Sample</th>
<th>ESR signal peak height</th>
<th>Averaged relative peak height</th>
<th>SOD-like activity (unit/g)</th>
<th>IC$_{50}$ (mg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOD (unit/ml)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.000</td>
<td>91.8</td>
<td>216.0</td>
<td>2.363</td>
<td></td>
</tr>
<tr>
<td>1.866</td>
<td>91.8</td>
<td>158.2</td>
<td>1.723</td>
<td></td>
</tr>
<tr>
<td>4.665</td>
<td>91.0</td>
<td>115.8</td>
<td>1.273</td>
<td></td>
</tr>
<tr>
<td>9.330</td>
<td>91.2</td>
<td>75.8</td>
<td>0.805</td>
<td></td>
</tr>
<tr>
<td>13.995</td>
<td>91.6</td>
<td>59.8</td>
<td>0.653</td>
<td></td>
</tr>
<tr>
<td>18.660</td>
<td>89.6</td>
<td>43.4</td>
<td>0.484</td>
<td></td>
</tr>
<tr>
<td>Raffinee (g/ml)</td>
<td>94.2</td>
<td>75.0</td>
<td>0.796</td>
<td>38,000</td>
</tr>
</tbody>
</table>

Calibration curve: $Y = 0.204054X - 0.059907; R = 0.996199$ where $Y = [Io/I]$, $X = $ SOD;
1 indicates the averaged relative peak height in various concentrations of SOD.

Figure 3. ESR signals of hydroxyl radical from DMPO-OH adduct without ascorbic acid. Mn$^{2+}$ signal as a standard.

A similar phenomenon occurred on the addition of Raffinee. The scavenger activity of Raffinee was obtained from the calibration curve by comparing the averaged relative peak height and that of standard ascorbic acid. 0.64 mg/ml of Raffinee causes approxi-
CLINICAL USE OF RAFFINEE IN CNS LESIONS

mainly the same effect as 0.516 mM of ascorbic acid (IC₅₀) with respect to inhibiting hydroxyl radical peak height by 50%. This result means that the hydroxyl radical scavenging activity of Raffinee is 790 units per gram, 7,900 units per potion (10 ml) (Table 4).

Table 4. Ascorbic Acid Activity Assay, Standard Data and Raffinee

<table>
<thead>
<tr>
<th>Sample</th>
<th>ESR signal peak height Mn²⁺ Radical</th>
<th>Averaged relative peak height</th>
<th>Hydroxyl radical scavenger activity</th>
<th>IC₅₀ (mg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascorbic acid (mM)</td>
<td>0.0</td>
<td>48.0</td>
<td>583.0</td>
<td>12.146</td>
</tr>
<tr>
<td></td>
<td>0.2</td>
<td>47.4</td>
<td>478.8</td>
<td>10.101</td>
</tr>
<tr>
<td></td>
<td>0.4</td>
<td>47.2</td>
<td>368.8</td>
<td>7.814</td>
</tr>
<tr>
<td></td>
<td>0.6</td>
<td>47.2</td>
<td>247.2</td>
<td>5.237</td>
</tr>
<tr>
<td></td>
<td>0.8</td>
<td>47.4</td>
<td>156.4</td>
<td>3.300</td>
</tr>
<tr>
<td></td>
<td>1.0</td>
<td>48.6</td>
<td>85.6</td>
<td>1.761</td>
</tr>
<tr>
<td>Raffinee (g/ml)</td>
<td>0.000612</td>
<td>47.8</td>
<td>310.0</td>
<td>6.485</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>7,900</td>
<td>0.64</td>
</tr>
</tbody>
</table>

Calibration curve: \( Y = 0.26143X + 0.25516 \) where \( Y = [\text{Ascorbic acid (mM)}], X = [\text{TeF} - 1] \).
1 indicates the averaged relative peak height in various concentrations of ascorbic acid.

The oral dosage of Raffinee in treatment of central nervous system (CNS) lesions was 2 potions 30 minutes before meals, 3 times a day. The components of Raffinee are easily absorbed by the alimentary tract. Daily doses of Raffinee contain 2,280,000 units superoxide radicals scavenging activity and 47,000 units hydroxyl radicals scavenging activity.

Case Presentations

Case 1

A 25 year-old female was admitted to the rehabilitation ward of Kaohsiung Medical College Hospital on Oct. 13, 1992, with the chief complaints of weakness and impaired sensation below the neck following a neck injury. She had a head injury without sequelae 3 years previously. On Sept. 8, thirty five days prior to admission, she suffered from a neck hyper-extension injury while playing games outdoors, and she felt weakness of the trunk and limbs and numbness below neck right after the trauma. She was sent to a local army general hospital and C7 bursting fracture with quadriplegia was noted. She received open reduction twice and internal fixation of C7 with iliac bone graft, then a rehabilitation program for spinal cord injury began. Twelve days after injury, she was transferred to the Veterans General Hospital in Kaohsiung. On Sept. 25, an MRI study of the cervical spine was done which revealed marked swelling with increased T2 weighted signal intensity of spinal cord from C4 to T1 (Figure 4A). A rehabilitation program continued in this hospital, but in vain.
On admission, she was moderately developed and clear though weak in appearance. Her mentality, motivation, and cooperation were good. Her general physical conditions were normal except quadriparesis. Hoffmann sign was negative bilaterally, Babinski sign was positive over the right side. Beever sign was negative. Superficial abdominal reflexes disappeared bilaterally. Her sphincter control and anal tone were preserved with positive bulbocavernous reflex. Deep tendon reflexes were increased over both lower limbs with mild clonus, and mild spasticity over the left leg, and moderate spasticity over right leg were noted. The muscle power below the C6 myotome was decreased accompanied by trunk muscle weakness (Table 5). There were hyperesthesia of pain, light touch, and vibration sensation below the C6 dermatome, and paresthesia below the C4 dermatome. Functionally she was confined to bed and totally dependent on caretakers.

Figure 4. MRI studies of cervical spine in case 1. Upper figure: marked cervical cord edema from C4 to T1 before Raffinee regimen (Sept. 25, 1992). Lower figure: remission of cervical cord edema after Raffinee regimen (Dec. 18, 1992).
CLINICAL USE OF RAFFINEE IN CNS LESIONS

After admission, a routine rehabilitation program for spinal cord injury started from bed activity training. The motor and sensory status remained the same as before one week following physical therapy and medication including prednisolone 30 mg per day, which was tapered and discontinued later on. Raffinee treatment started 10 days after admission with standard dosage for CNS lesions for 6 weeks. Two weeks after this intervention, motor recovery of the upper limbs began to be noted. The speed of improvement of motor and sensory status was so dramatic that nearly full motor and sensory recovery was obtained within one month of treatment (Table 5). The accompanying functional recovery was also marked. Four weeks after Raffinee treatment, she could stand on a tiling table and overcome postural hypotension, then progressively she could achieve independent wheelchair activity, ambulate with a regular cane, and eventually walk around without any devices. Follow-up MRI study of cervical spine done on Dec. 18 revealed complete remission of cervical cord edema (Figure 4B). She was discharged on Jan. 30, 1993 and walked away from the ward with very mild spastic gait involving the right leg. Two years of follow-up showed that her motor and sensory functions maintained a high level of function.

Table 5. Improvement of Muscle Powers in Case 1

<table>
<thead>
<tr>
<th>Right side</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>12/18</td>
<td>11/23</td>
<td>11/7</td>
<td>10/19</td>
<td>10/13</td>
<td>10/13</td>
<td>10/19</td>
<td>11/7</td>
<td>11/17</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>C4</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>C5</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>C6</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>5</td>
<td>3</td>
<td>3</td>
<td>C7</td>
<td>4</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>C8</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>T1</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>4.5</td>
<td>4</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>L2</td>
<td>3</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>4.5</td>
<td>4</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>L3</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>4.5</td>
<td>4</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>L4</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>4.5</td>
<td>4</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>L5</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>4.5</td>
<td>4</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>S1</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>

0: no contraction felt; 1. muscle can be felt to tighten but cannot produce movement; 2. produce movement with gravity eliminated but cannot function against gravity; 3. can raise part against gravity; 4. can raise part against outside resistance as well as against gravity; 5. normal condition.

Case 2

A 53 year-old woman was sent to the emergency room of Cheng-Ching Hospital in Taichung due to sudden onset of loss of consciousness on July 21, 1993. Emergent CT scanning study of the brain showed right cerebellar hemorrhage, measuring 2.5 cm x 2.5 cm x 2 cm. She had had hypertension and underwent regular treatment for several years. The comatose state lasted for 3 days when she was cared for in an intensive care unit. Her vital signs were kept stable and she regained consciousness on the fourth day of hospitalization. She could move her limbs but severe headache and dizziness made her unable to sit up.
Raffinone treatment started on the day she became conscious with the standard dosage for CNS lesions for 4 weeks. Headache and dizziness subsided dramatically 3 days after the regimen, and she could stand up without support. The duration of hospitalization was only one week. She regained mobility so fast that she could walk around freely and achieve an independent living 2 weeks after discharge. There appeared to be no sequel of this episode of cerebellar hemorrhage during the subsequent 3 years of follow-up.

Discussion

High doses of methylprednisolone administered within 8 hours after spinal cord injury improved neurologic function (Bracken et al., 1990). This exciting report opened the new era of aggressive treatment of acute CNS lesions. The most likely explanation for the observed effects of treatment is that methylprednisolone suppresses the breakdown of membrane by inhibiting lipid peroxidation and hydrolysis at the site of injury. In Japan (Asano et al., 1996), a multicenter, placebo-controlled double-blind trial of a hydroxyl radical scavenger AVS ((+-)N,N' propylene-dimicotoamin; nicaraven) proved that the agent significantly ameliorated delayed ischemic neurological deficits (DINDs) following aneurysmal subarachnoid hemorrhage (SAH). DINDs result from vasospasm following various cerebrovascular accidents, especially SAH. The liberation of oxyhemoglobin into the cerebrospinal fluid (CSF) on lysis of the red blood cells is the primary cause of vasospasm (Macdonald et al., 1991; Peterson et al., 1990), and the participation of lipid peroxidation in the occurrence of vasospasm has been supported by numerous reports (Steele et al., 1991; Watanabe et al., 1988). Membrane lipid peroxidation mediated by hydroxyl radicals strongly contributes to the secondary injury of CNS lesions.

In neural cells of the central nervous system, the concentrations of antioxidant enzymes are lower and the content of iron is higher than other cells. The concentration of vitamin C in CSF is 10 times of that in serum. During CNS lesions, neurons are damaged and release a large amount of iron into the CSF. Iron is oxidized to ferrous ion by vitamin C. Through the Fenton reaction, hydroxyl radicals are produced by the reaction of ferrous ions and hydrogen peroxides. In addition, vasospasm occurs and focal ischemia develops. During reperfusion, xanthine oxidase oxidizes reenter oxygen into superoxide radicals, then superoxide radicals react with hydrogen peroxides to produce hydroxyl radicals (Harber-Weiss reaction). Hydroxyl radicals then attack unsaturated fatty acids of other neuron cell membrane by lipid peroxidation and cause cell death by damaging cell membranes (Gutteridge, 1995). Another pathway of hydroxyl radical production during CNS lesions is mediated by glutamate. A large amount of glutamates are released from damaged neurons. Glutamates will combine with NMDA (N-methyl-D-aspartate) receptors on the membrane of adjacent neurons and induce influx of Ca$^{2+}$ into those cells (Choi, 1990). The massively influxed Ca$^{2+}$ ions combine with calmodulin, then activate constitutional nitric oxide synthetase, which catalyzes formation of nitric oxide radical from oxygen and L-arginine. Nitric oxide radical and superoxide radical will react to form hydroxyl radical in acidic condition (Lipton et al., 1993). Secondary injury begins within 1 hour after the initial lesion. The vicious cycle of lipid peroxidation may even last for days (Tator and Fehlings, 1991; Young, 1993).
CLINICAL USE OF RAFFINEE IN CNS LESIONS

Raffinee was proved by ESR spectrometry to have high superoxide radical scavenging effect (380,000 unit/potion) and hydroxyl radical scavenging effect (7,900 unit/potion). The standard dosage of Raffinee regimen used in this report is equivalent to 2,280,000 units of superoxide radical scavenging activity and 47,400 units of hydroxyl radical scavenging activity.

In both cases, the process of the cascade of lipid peroxidation seemed to resume until the beginning of Raffinee regimen. In case one, persistent cervical cord edema and delayed motor recovery might stand for the existence of hydroxyl radical inducing lipid peroxidation cascade. In case two, severe headache and dizziness might represent the stage of vasospasm following cerebellar hemorrhage. The dramatic therapeutic responses of both cases may indicate that in subacute stage of CNS lesions, Raffinee is an effective agent to restore neuron function in the ischemic zone by scavenging superoxide and hydroxyl radicals. Further randomized, placebo-controlled, double-blind large scale clinical study is necessary to verify this efficacy.

References


H. Y. CHEN et al.


