E2-19: Bioactivity of phenolic constituents from *Vernonia cinerea*

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Vernonia cinerea (F Asteracea, *Sinh.* Monera Kudumbiya, *Tam.* Puvam Kurundal) is a small herb used in Sri Lanka, in the treatment of liver disease. Several highly active phenolic compounds which inhibit the respiratory burst activity of activated polymorphonuclear leukocytes (PMNL) have been reported from the plant. The inhibition of PMNL's could be of therapeutic significance in certain inflammatory conditions. The results of further studies on the active phenolic compounds isolated from *Vernonia cinerea* are reported in this paper.

The activity of PMNL was assayed by measuring the chemiluminescence generated in the presence of luminol, when the respiratory burst is triggered *in vitro* by opsonized zymosan particles. The inhibitory activity of the compounds are conveniently expressed as IC_{50} values, i.e. the concentration required to produce a 50% reduction in chemiluminescence with respect to a control (zero concentration of compound. (*Table I*).

All the compounds in *Table 1*, exhibited a dose dependent inhibition of chemiluminescence. It is necessary to differentiate between specific inhibition of respiratory burst activity from general cytotoxicity. This was carried out by pre-incubating the PMNL with the test compounds, and assaying their activity in the absence of the compound. All compounds with the exception of iuteolin-7-0-glucoside, were non cytotoxic.

The reduction of chemiluminescence could also be due to the scavenging of reactive oxygen species, rather than the inhibition of their generation. The scavenging of $O_2^{\cdot-}$ was examined by observing the influence of test compounds on the $O_2^{\cdot-}$ dependent, superoxide dismutase inhibitable reduction of cytochrome C. Superoxide anion was generated by the xanthine oxidase catalysed conversion of hypoxanthine to uric acid. As shown in table 1, luteolin and its glucosides scavenge 30% of $O_2^{\cdot-}$, while the scavenging by caffeic acid derivatives is much less. However, luteolin also inhibits xanthine oxidase activity. Therefore the actual scavenging would be less than 30%.

It could be concluded that all the compounds tested are genuine inhibitors of the generation of reactive oxygen species by activated PMNL.

It is of interest to note that the caffeoyl moiety which is found explicitly in compounds **IV** to **VIII**, is an implied substructure in compounds **I** to **III**.

Compound	IC_{50} (M)x10^5	% Inhibition of rate of reduction of cytochrome C
Luteolin (I)	$(8.7 \pm 1.7) \times 10^{-1}$	30 ± 3
Luteolin-7-O-glucoside(II)	1.0 ± 0.2	25 ± 2
Luteolin-4^1-O-glucoside(III)	5.6 ± 2.2	28 ± 2
Chlorogenic acid(IV)	1.3 ± 0.1	13 ± 2
[3,5] Dicaffeoyl quinic acid(V)	1.3 ± 0.2	9 ± 2
[3,4] Dicaffeoyl quinic acid(VI)	1.7 ± 0.3	9 ± 2
[4,5] Dicaffeoyl quinic acid(VII)	1.7 ± 0.3	9 ± 2
Methyl caffeate(VIII)	2.5 ± 2.2	11 ± 2

Table 1 IC_{50} values and scavenging activity of phenolic compounds isolated from *Vernonia cinerea* (n = 4, ± 1 s.d.)