STUDIES ON CLINICAL EFFECTS OF GINSENG: 2ND REPORT; EFFECTS OF GINSENG AT ACUTE MASSIVE DOSAGE ON CIRCULATORY FUNCTION—A STUDY BY DIGITAL PLETYSMOGRAPHY

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Introduction

In a previous double blind study of Ginseng Radix-rubra, we called it KGC, to determine its efficiency in alleviating symptoms, we found that Ginseng medication resulted in marked improvement of symptoms associated with circuratory disturbances (eg., headache stiff shoulder in patients with arteriosclelosis and coldness of the limb in patients with hypotension).

Accordingly, we investigated the effects of KGC on circulatory function in healthy adults by means of digital pletysmography (DPG) which has been shown to accurately represent heart function and periferal hemodynamics.

Meterials and methods

The test drug and placebo used were the same as those described in the first report.

The oral, single dose administration of 10 capsules (equivalent to 3.0 g of Ginseng Radix rubra powder) was administrated as a experimental drug.

Table 1 shows the background of the subjects. All subjects were healthy volunteers, and were allocated to the KGC-dosed or placebo-dosed group such that their background would not influence the results.

Table 1. Background of Subjects

1) KGC group:	8 male, 8 female
	22 ~ 36 years in age,
	28.3 ± 5.5 years SEM
2) Placebo group:	5 male, 5 female
	21 ~ 39 years in age,
	29.3 ± 6.6 years SEM

no significant difference were found between 2 groups

Mesurement by DPG

DPG was performed before and 1 hour after the oral administration of KGC or placebo for hemodinamic study.

The preamplifier, we had used to obtain DPG is the Fukuda Electronics model PT-300 photopletysmography. The recorder is the model FD-20 2-channel electrocardiograph.

The procedure for DPG how to obtain the hemodinamic index, and its significance are il-

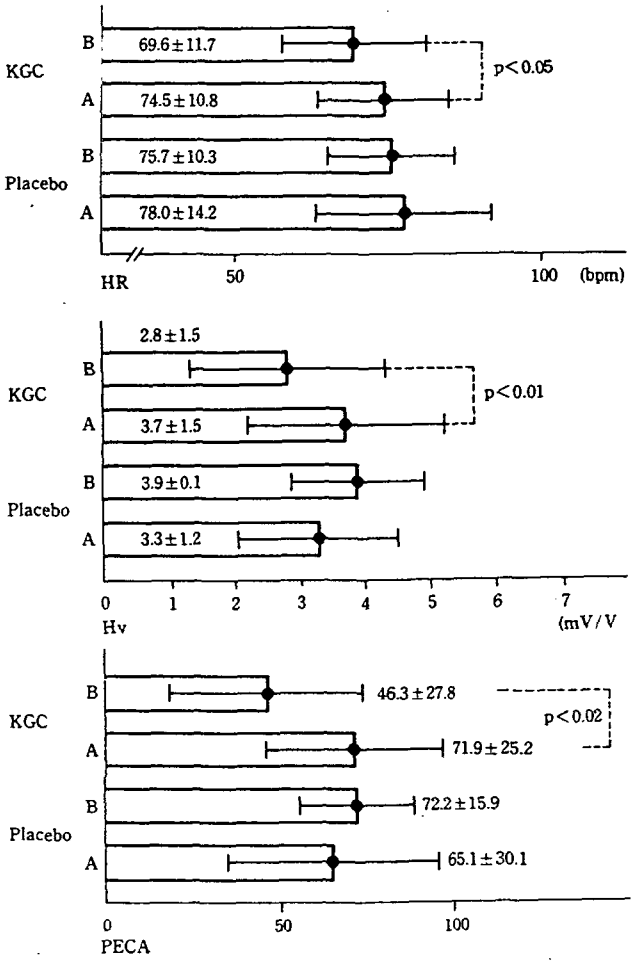


Fig. 1. Parameters for Cardiac Output and Peripheral Circulation.

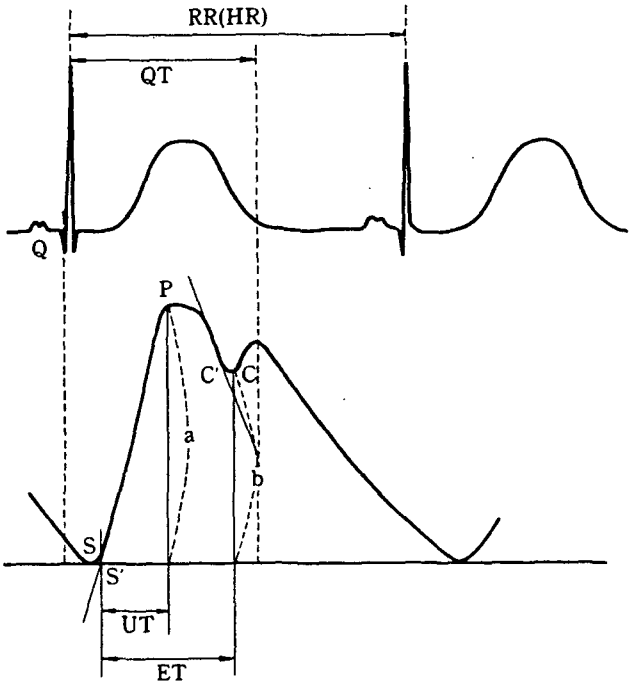
lustrated on Table 2.

The cardiac output and periferal hemodinamic parameters used included the heart rate (HR), the height of volluka (HV), and the peripheral effects of cardiac beat action (PECA).

Isovolumic contraction time (ICT) and a ratio of left ventricular ejection time to isovolumic contraction time (ET/ICT) was used as parameters for cardiac muscle contractility.

The parameters for peripheral vascular resistence (after load) and distension consisted of the coefficient of incisura (CI) and the upstroke time (UT).

Table 2. Measurement of DPG and Procedure to obtain various Hemodynamic Index



Each index are calculated as follows
ET/ICT ≒ ET/QT − ET
PECA = Hv/Hvs* × HR
*Hvs = Volluka standard in healthy young (4.0m V/V) by Yoshimura
CI = b/a
HR, HV, PECA were used as parameters for cardiac output and peripheral circulation . . . . . Yoshimura[2,6] et al. ICT, ET/ICT were used as parameters for cardiac contractility . . . Aronow et al.[3,4] CI, UT were used as parameters for peripheral vascular resistance and distension . . . Yoshimura[2], Freis[5] et al.

Results

Fig 1 shows changes in HR, HV and PECA after the medication with the test drug, compared with the pretreatment values. In the KGC-dosed group, HR, HV and PECA all exhibited significant increases at a 95–99% level, while in the placebo-dosed group these parameters remained unchanged.

Fig 2 showes changes in ICT and ET/ICT. In the KGC-treated group a tendency to the reduction in ICT and a tendency to the increase in ET/ICT were noted after the treatment, whereas no changes were found in the placebo-dosed group.

Changes in UT and CI are shown in Fig 3.

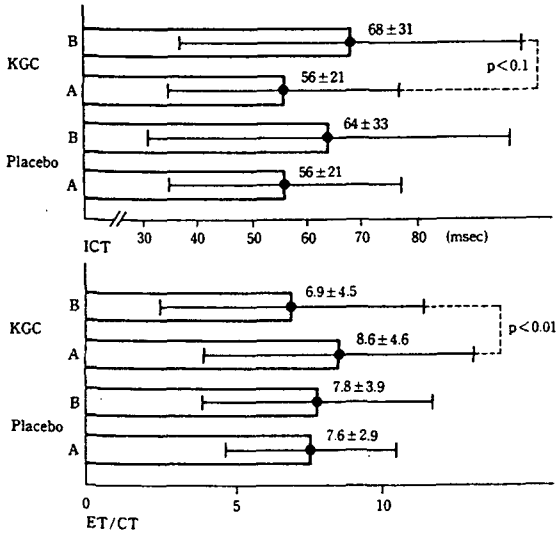


Fig. 2. Parameters for Cardiac Muscle Contractility

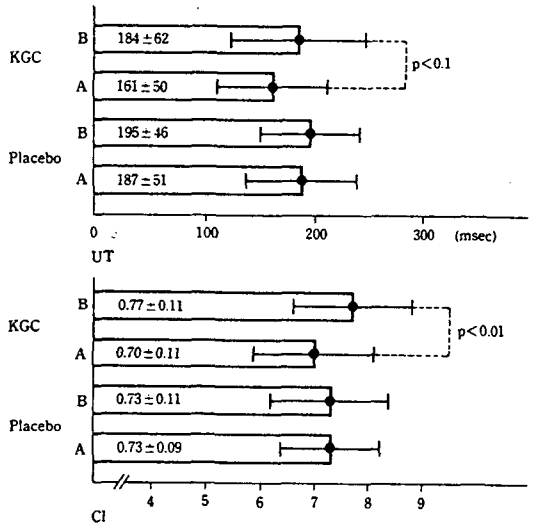


Fig. 3. Parameters for Peripheral Vascular Resistance (after load) and Distension.

In the KGC-dosed group a tendency to the reduction in UT and a reduction in CI were noted, while in the placebo-dosed group no such a changes were observed.

The original data shown on Table 3.

Table 3. Original Data which were obtained by DPG method

	Case No.	Age (yrs.)	Sex	HR(bpm) B	HR(bpm) A	Hv(my/V) B	Hv(my/V) A	PECA B	PECA A	QT(msec) B	QT(msec) A	ET(msec) B	ET(msec) A	ICT(msec) B	ICT(msec) A	ET/ICT B	ET/ICT A	UT (msec) B	UT (msec) A	CI B	CI A
	1	23	F	82	77	2.0	4.8	41.0	92.4	421	453	374	363	47	90	8.0	4.0	164	159	0.70	0.67
	2	22	M	52	60	2.3	5.1	30.0	75.0	409	450	335	400	74	50	4.5	8.0	93	160	0.83	0.67
	3	35	M	63	58	4.4	5.2	69.0	75.4	402	432	348	354	54	78	6.4	4.5	143	138	0.73	0.77
	4	22	F	70	85	0.4	4.0	7.0	73.0	432	452	360	428	72	24	5.0	17.8	108	119	0.50	0.50
	5	26	F	58	65	0.4	3.0	5.8	48.8	425	416	393	374	32	42	12.3	8.9	138	123	0.83	0.75
	6	26	M	57	65	5.6	3.2	79.0	52.0	372	353	351	334	21	19	16.7	17.5	234	125	0.86	0.82
K	7	36	M	75	90	5.2	5.3	97.5	119.3	450	441	358	392	92	49	3.9	7.3	201	147	0.77	0.61
G	8	36	M	62	74	2.8	3.6	43.4	55.5	406	399	325	355	81	44	4.0	8.1	122	111	0.86	0.81
C	9	23	F	61	73	1.0	3.2	15.3	58.4	447	441	323	353	124	88	2.6	4.0	121	132	0.80	0.44
	10	33	F	69	77	4.8	6.4	82.8	123.2	459	453	386	408	73	45	5.3	9.1	257	272	0.75	0.81
	11	31	M	79	75	3.0	4.0	59.3	77.0	413	447	367	402	46	45	8.0	8.9	275	268	0.87	0.80
	12	36	M	89	90	2.2	1.3	49.0	29.3	438	416	341	343	97	73	3.5	4.7	146	122	0.73	0.71
	13	31	M	57	63	0.8	4.2	11.4	63.0	417	450	294	369	123	81	2.4	4.6	234	143	0.88	0.71
	14	26	F	85	93	2.8	5.0	59.5	93.0	476	498	405	423	71	75	5.7	5.7	262	174	0.71	0.64
	15	23	F	70	73	2.4	3.3	42.0	60.2	388	397	367	353	21	44	17.4	17.0	259	154	0.92	0.81
	16	24	F	85	75	2.3	2.9	48.9	54.4	476	492	405	410	71	50	5.7	8.0	190	223	0.65	0.69
	17	39	M	79	77	5.0	2.4	98.8	46.2	459	453	367	385	92	68	4.0	5.7	207	181	0.76	0.75
P	18	21	F	73	63	3.2	2.4	58.4	37.8	441	410	353	348	88	62	4.0	5.6	155	143	0.56	0.75
L	19	36	F	80	90	2.2	2.6	44.0	58.5	462	490	416	440	46	50	9.0	8.8	208	245	0.67	0.64
A	20	39	M	67	73	4.4	3.9	73.7	73.1	432	397	338	353	94	44	7.7	8.0	254	132	0.91	0.82
C	21	23	F	80	95	3.9	5.4	78.0	128.3	462	453	338	402	124	51	2.7	7.9	139	151	0.67	0.56
E	22	23	F	70	76	4.0	4.0	70.0	76.0	432	428	389	335	43	93	9.0	3.6	151	180	0.63	0.65
B	23	27	F	57	52	4.8	2.8	68.4	32.9	326	391	300	352	26	42	11.5	8.4	273	298	0.88	0.89
O	24	31	M	95	98	3.8	4.0	90.3	83.0	453	394	392	357	60	37	6.5	9.6	151	153	0.67	0.70
	25	28	F	73	72	4.4	4.4	80.3	83.6	419	438	375	351	40	87	9.4	4.0	221	175	0.81	0.76
	26	32	M	83	84	2.9	1.5	60.2	31.5	453	456	423	426	30	30	14.1	14.2	188	213	0.76	0.75

[Note] B: Before, A: After administration

Discussion and Summary

The first accounts of the effects of Ginseng Radix rubra on circulatory function dates back to the time of Pen Tao Song-gu, who described its cardiotonic effect.

Modern pharmacologic studies of Ginseng Radix rubra have been extensively conducted since the 1950's, and many beneficial and therapeutic effects have been attributed to the drug as a result of these investigations.

Kim reported that of 2 of the saponin components of Ginseng Radix rubra, ginsenoside-Rb_1 and ginsenoside-Re, the former has an epinephrin-like action that increases the contractile power of cardiac muscles through its positive inotropic action, while the latter acts as antagonist that blocks epinephrin receptors.

He presented evidence that the action of ginsenoside-Rb_1 on the cardiac muscles under perfusion was inhibited by such epinephrin antagonists as propranorol and reserpine and that epinephrin failed to exert its positive inotropic action on the cardiac muscles when pretreated with ginsenoside-Re. He further indicated that although a previous report attributed a cardiac power inhibitory action to Ginseng Radix rubra, this phenomenon presented itself only when the drug was used at an extremely large dose, and concluded that in spite of the coexistent agonists antagonists *in vivo,* Ginseng Radix rubra at aphysiological concentration exerted a mild cardiac stimulating effect.

In recent years, Lee and Kim have reported the inhibition of the concentration of peripheral smooth muscle through Ca^{++} antagonism, which calls attention to its direct effect on blood vessels. In analysis of the effects of Ginseng Radix rubra based on the findings from the present study, the decrease in CI and the tendency toward reduction in UT appeared to represent a tendency toward the dilatation of peripheral blood vessels due to a direct action of the drug on blood vessels and subsequently leading to reduced peripheral vascular resistance. The increase in HR, reduction in ICT, and the increase in ET/ICT appear to have been the result of a mild cardiotonic effect of the drug.

Such a reduction in after-load and an increase in cardiac muscle contraction may be presumed to result in an increase in cardiac output and in improvement in peripheral circuration. This was supported by the increase in HV and PECA.

Moreover, these conclusion are in accord with the results of the aforementioned basic experiments conducted by Kim et al. These findings further suggest that Ginseng Radix rubra may be clinically useful as an agent for improvement of peripheral circulation and as a therapeutic agent for cardiac failure when used in conjuction with cardiotonic glucosides and for many other cardiovascular diseases.