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RESEARCH ARTICLE

EFFECTS OF ADMINISTRATION OF ETHANOLIC EXTRACT OF *GANODERMA LUCIDUM* ON ARTERIAL BLOOD PRESSURE OF NORMOTENSIVE CATS.

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Key words:-

Ganoderma lucidum; fruiting bodies, normotensive, arterial blood pressure; Atropine, Ach, Propranolol.

Abstract

The fruiting bodies ethanol extract of *Ganoderma lucidum* of the family *Ganodermataceae* was evaluated for arterial blood pressures lowering effects in normotensive cats. The effects of each dose of extract on the arterial blood pressure (BP) of normotensive cats were studied. The extract exhibited a significant ($p < 0.05$) dose-dependent depression of blood pressure in normotensive cats between 1, 10 and 50 mg/ml. It produces a decrease in systolic blood pressure ($p < 0.05$ value). It also exhibited a decrease in diastolic pressure which was significant ($p < 0.05$) at all three doses. On mean arterial blood pressure (MABP), *Ganoderma lucidum* has a decreasing effect, which is statistically significant. The activities of the extract were comparable to that of other reference drugs: propranolol, Ach, and Atropine sulphate. The intravenous LD₅₀ value of the extract was 12.89 mg/kg body weight in mice (MEDEP, 2008). The results obtained from the present studies supported the traditional claim that the plant is used in the management of hypertension in human.

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Introduction:-

Ganoderma lucidum is a member of the family *Ganodermataceae*, the kingdom of fungi, the division of Basidiomycota, the class of homobasidiomycetes, the order of aphyllphorales, and the genus of *Ganoderma* (Chang, 1999).

Ganoderma lucidum is a fungi that has potentially shown potency in its use by traditional herbalist, elites and emperors in Korea, Japan and china and even locally here in Nigeria (Ofodile et al., 2005). Mushrooms have a notable place in the folklore through the world and in the tradition of many culture (chang and Bushwell, 1996). The family of *Ganodermataceae* consists of a large group of tree fungi of the class *polyporaceae*, specifically the genus *Ganoderma* and other related genera. *Ganoderma* fungi are mainly found in tropical and subtropical areas; the typical species is *Ganoderma lucidum* (Fr.) Karst. It is called Ling Zhi or Reishi (Chinese), Mannentake (Japanese) and Tuwon biri (Hausa). It is seasonal and can be found growing alone or in group on decaying hardwood logs and stumps. At first, the caps are irregularly knobby or elongated, but by maturity more or less fan-shaped; with a shiny, varnished surface often roughly arranged into lump "Zones", red to reddish brown when mature; when young often with Zones of bright yellow and white toward the margin. The stem is sometimes absent, but more commonly

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present; 3-14cm long up to 3cm thick; twisted; equal or irregular; varnished and colored like the cap; often distinctively angled away from one side of the cap. The under side is cream colored and porous. *G. lucidum* is commonly known as a medicinally-potent mushroom. It has been widely used in China and other oriented countries for hundreds of years for treatment of various diseases, including cancer. This mushroom is reported to have various biological activities, such as anti-tumor, anti-bacterial and anti-viral activities (Yoon et al., 1994; Wang et al., 1997; El-Mekkawy et al., 1998; Eo et al., 2000). It was also reported to have an anti-inflammatory and liver protective effect in rats (Lin et al., 1993; Lin et al., 1995).

Some medicinal uses of *Ganoderma lucidum* include anti-tumor, immunomodulatory, immunotherapeutic, anti-inflammatory, antiviral, anti-parasitic, anti-fungal, antidiabetic, and hepatoprotective activities. It has also been found to inhibit platelet aggregation, and to lower blood pressure, cholesterol and blood sugar. Because of these properties, lingzhi has been regarded as a blood pressure stabilizer, antioxidant, analgesic, a kidney and nerve tonic. It has been used in bronchitis prevention and in the treatment of high triglycerides, high blood pressure, hepatitis, allergies, chemotherapy support, HIV support, and even for fatigue and altitude sickness (Paterson, 2006). More recently, environment and culture media have been investigated with regards to the effect they have on the extracellular or intracellular bioactive components found in the mycelium of *Ganoderma lucidum* (Fang et al., 2002; Kim et al., 2002; Lee et al., 2004).

The present day study was aimed at evaluating the anti-hypertensive activity of the plant in cats in order to support or refute the claims by traditional herbalists.

Materials and Methods:-

Plant Material Identification:-

A sample of *Ganoderma lucidum* (fruiting body) was collected around Ahmadu Bello University Zaria in February, 2008. The plant was identified and authenticated by M. Musa of the herbarium section in the department of Biological Sciences, Ahmadu Bello University Zaria. A herbarium specimen was prepared and deposited there with a voucher number of 005.

Extraction of Plant Material:-

The extraction of the fruiting body *Ganoderma lucidum* was carried out in the department of Pharmacognosy, Faculty of Pharmaceutical Science, Ahmadu Bello University, Zaria. 500g of the fruiting body of *Ganoderma lucidum* was dried and weighed using a weighing balance. It was then pounded in to powdery form using a hammer mill. 300g of the powdery *Ganoderma lucidum* was mounted on the Soxhlet apparatus and extracted using 1 litre of ethanol (95%) to obtain a brown liquid. The extract is poured into an evaporating dish to evaporate it over a water bath to dryness at temperature range of 40-50°C for 1 hour to obtain the crude extract. About 15g of the crude extract was obtained.

Experimental Animals:-

The experimental animals, cat (male) weighing 1.262 kg and 2.300 kg was purchased in Samaru market in Zaria, Nigeria and was kept in the animal house of the department of Pharmacology and Clinical Pharmacy, Ahmadu Bello University, Zaria under normal physiological condition and room temperature for 3 days to acclimatize. Animal was given normal diet and water, but was deprived of food prior to the experiment at least for 10 hours.

Acute Toxicity Study:-

The method of Lorke (1980) was adopted and a total of 24 rats weighing 120-145g each were used for this study. The animals were fasted for 12hrs before the study, but were allowed water *ad libitum*. In the initial phase, four groups (n=3) were given normal saline as control group and 100, 1000, and 10,000 mg/kg of the extract intraperitoneally (*i.p*) for the remaining three groups respectively. They were then observed for 24hrs for signs of toxicity or deaths. In the final phase, another four groups (n=3) were given normal saline, 2000, 4000 and 8000 mg/kg of the extract *i.p* for the remaining groups respectively and were observed for signs of toxicity or deaths. The median lethal dose (LD₅₀) was calculated from the final phase.

Test for hypotensive study:-

The cats (1.262kg and 2.300kg) used were anaesthetized using thiopental sodium 45 mg/kg. Complete anesthesia was obtained after about 45 minutes, and the cat was placed in a dorso-ventral position on a dissecting table which was previously heated electrically to maintain the body temperature of the animal. The femoral vein of the cat was

then dissected and canulated (insertion of a small tube into the vein through which drugs are directly injected into the circulation). The neck region of the cat was the shaved with scissors and the carotid artery was canulated and connected to a pressure transducer and the pressure was raised by means of a syringe to the expected blood pressure of the animal. The arterial canula was connected to the recording microdynamometer. Injection of drugs and extract were made starting with physiological normal saline and the response obtained on UGO basile graph sheet. The experiment was repeated twice.

Statistical Analysis:-

Results were expressed as Mean \pm Standard Error of Mean (SEM). The data was statistically analyzed using the one-way ANOVA to determine whether the result were significantly different from those in the corresponding control group followed by turkey multiple test comparison. The results were statistically significant when P values are less than 0.05 ($p < 0.05$) as described by Duncan et al (1977).

Results:-

The extract was found to have a significant ($p < 0.05$) and dose-dependent hypotensive effect at doses of 1, 10 and 50 mg/ml as it decreases the systolic and diastolic blood pressure in normotensive cats (Table 1 and 2). The highest decrease displayed by the extract at a dose 50 mg/ml was comparable to that of normal saline 0.9w/v. All values obtained were significant $p < 0.05$ in comparison with the negative control.

The extract was also found to have little or no effect on the amplitude of the pulse pressure and a decreasing effect that was statistically significant ($p < 0.05$) on the MABP.

Table 1:- The systolic blood pressure after administration of normal saline, standard drug and various concentrations of Ganoderma lucidum extract.

S/NO	Volume administered (ml)	Normal saline 0.9w/v (control)	Extract 1mg/ml	Extract 10mg/ml	Extract 50mg/ml	P-value
		Means \pm SEM	Means \pm SEM	Means \pm SEM	Means \pm SEM	
1	0.1	65.50 \pm 5.50	69.50 \pm 5.50	66.00 \pm 5.00	51.50 \pm 4.50	0.153 ^{ns}
2	0.2	71.00 \pm 10.00	74.50 \pm 9.50	61.00 \pm 0.00	53.00 \pm 1.00	0.030 ^a
3	0.4	71.50 \pm 10.50	74.00 \pm 11.00	57.50 \pm 0.50	48.50 \pm 1.50	0.015 ^a
4	0.8	68.00 \pm 11.0	73.00 \pm 10.00	50.00 \pm 5.00	44.00 \pm 4.00	0.009 ^a

a=statistically significant, ns = statistically not significant.

Ganoderma lucidum has a decreasing effect on the systolic blood pressure that is dose dependent at constant volume.

Table 2:- The diastolic blood pressure after administration of normal saline, standard drugs and various concentrations of Ganoderma lucidum extract.

S/NO	Volume administered (ml)	Normal saline 0.9% w/v (control)	Extract 1mg/ml	Extract 10mg/ml	Extract 50mg/ml	P-value
		Mean \pm SEM	Mean \pm SEM	Mean \pm SEM	Mean \pm SEM	
1	0.1	36.00 \pm 5.00	44.00 \pm 0.00	40.50 \pm 0.50	26.50 \pm 4.50	0.040 ^a
2	0.2	40.00 \pm 9.00	46.00 \pm 2.00	37.50 \pm 1.50	31.00 \pm 3.00	0.013 ^a
3	0.4	39.50 \pm 8.50	46.00 \pm 3.00	34.50 \pm 2.50	28.00 \pm 5.00	0.014 ^a
4	0.8	35.50 \pm 5.50	45.00 \pm 3.00	27.50 \pm 8.50	24.00 \pm 7.00	0.014 ^a

a=statistically significant, ns=statistically not insignificant.

Ganoderma lucidum has a decreasing effect on the diastolic blood pressure that is dose dependent at constant volume ($p < 0.005$ value). The change produced by Ganoderma lucidum at dose concentration 1mg/ml, 10 mg/ml and 50 mg/ml are all statistically significant ($p < 0.05$).

Table 3:- The pulse pressure after administration of normal saline standard drugs and various concentrations of Ganoderma lucidum extract.

S/NO	Volume administered (ml)	Normal saline 0.9w/v	Extract 1mg/ml	Extract 10mg/ml	Extract 50mg/ml	P-value
		Mean± SEM	Mean± SEM	Mean± SEM	Mean± SEM	
1	0.1	29.50±0.50	25.50±5.50	25.50±4.50	25.25±0.25	0.916 ^{ns}
2	0.2	31.00±1.00	28.50±7.50	23.50±1.50	22.00±2.00	0.474 ^{ns}
3	0.4	32.00±2.00	28.00±8.00	23.00±2.00	20.50±3.50	0.309 ^{ns}
4	0.8	32.50±5.50	28.00±7.00	22.50±3.50	20.00±3.00	0.333 ^{ns}

a=statistically significant, ns=statistically not significant.

Ganoderma lucidum has little or no effect on the amplitude of the pulse pressure. at volumes of 0.1 ml, 0.2 ml, 0.4 ml and 0.8 ml. They produce changes in the pulse pressure that is statistically insignificant.

Table 4:- The mean arterial blood pressure of normal saline, standard drugs and various concentrations of Ganoderma lucidum extract.

S/NO	Volume administered (ml)	Normal saline 0.9% w/v (control)	Extract 1mg/ml	Extract 10mg/ml	Extract 50mg/ml	P-value
		Mean± SEM	Mean± SEM	Mean± SEM	Mean± SEM	
1	0.1	45.85±5.15	52.50±1.80	49.00± 2.00	34.86±4.50	0.061 ^{ns}
2	0.2	50.35 ± 9.35	55.50±4.50	45.30± 1.00	38.35±2.35	0.016 ^a
3	0.4	50.15 ± 9.15	55.35±5.65	42.15± 1.85	34.85±3.85	0.011 ^a
4	0.8	46.35 ± 7.35	54.35±5.35	35.00± 7.30	30.70±6.00	0.010 ^a

a=statistically significant, ns=statistically not significant

On mean arterial blood pressure (MABP), G. lucidum has a decreasing effect, that is statistically (p<0.05) significant at volumes of 0.2 ml, 0.4 ml, 0.8 ml

Result of drug antagonistic studies on Ganoderma lucidum extract:-

Table 5:- Interactions of 0.8 ml extract 10 mg/ml with standard drugs showing systolic, diastolic, pulse and mean arterial blood pressure

S/No	Blood pressure (mmHg)	0.2ml Propranolol 4mg/ml + 0.8ml extract 10mg/ml		0.2ml atropine 100ug/ml + 0.8ml extract 10mg/ml	
		MEANS±SEM		MEANS±SEM	
		Before	After	Before	After
1.0	Systolic	60.50±10.50	48.00±6.00 ^{ns}	58.50±7.50	50.00±5.00 ^{ns}
2.0	Diastolic	40.50±8.50	26.50±0.50 ^{ns}	35.00±5.00	25.00±3.50 ^{ns}
3.0	Pulse	20.00±2.00	21.50±5.50 ^{ns}	23.50±2.50	24.50±1.50 ^{ns}
4.0	Mean Arterial	47.15±9.15	33.65±2.35 ^{ns}	42.85±5.85	33.70±4.00 ^{ns}

a=statistically significant, ns=statistically not significant.

Discussions:-

The fruiting body ethanol extract of Ganoderma lucidum had demonstrated a significant (p<0.05) and dose-dependant hypotensive activity. This was evident as it reduces systolic, diastolic, pulse and mean arterial blood pressure parameters significantly.

From the results, normal saline 0.9%w/v was used as the control, while the standard drug used are Acetylcholine (1µg/ml), Propranolol (4mg/ml) and Atropine (100 µg/ml). This was then used in the experiment to compare with the extract which is the ethanolic extract of Ganoderma lucidum of dose concentrations, 1mg/ml, 10mg/ml and 50mg/ml respectively.

From the tables above Ganoderma lucidum has a decreasing effect on the systolic blood pressure that is dose dependent and statistically significant, at constant volume, Ganoderma lucidum causes a decrease in the systolic

blood pressure that is dose- dependent. It produces a decrease in systolic blood pressure as low as 69.50 ± 5.5 mmHg, 50.00 ± 5.00 mmHg and 44.00 ± 4.00 mmHg at concentration of 1mg/ml, 10 mg/ml and 50 mg/ml of *Ganoderma lucidum* extract respectively compared with 65.50 ± 5.50 mmHg for normal saline 0.9% w/v (p value), but this effect is lower than the effect produced by 0.8 ml acetylcholine (1 μ g/ml), 38.50 ± 4.50 mmHg.

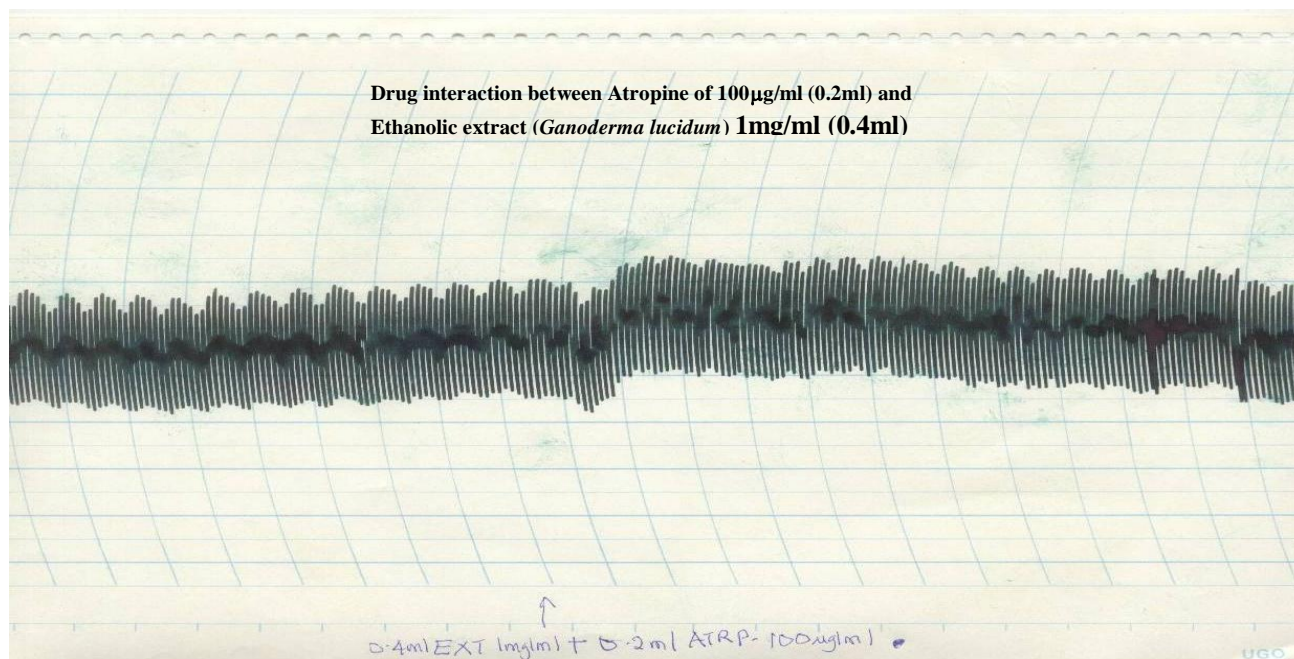
Ganoderma lucidum has a high statistically significant decreasing effect on the diastolic blood pressure that is dose dependent at constant volume (P-value). Producing as low as 44.00 ± 0.00 mmHg, 27.50 ± 8.50 mmHg and 24.00 ± 7.00 mmHg for concentrations of 1mg/ml, 10 mg/ml and 50 mg/ml respectively as against $35.50 \pm$ mmHg produced by normal saline 0.9% w/v. this blood pressure lowering effect is lower than that produced by 0.4 ml acetylcholine (1 μ g/ml) 11.50 ± 8.50 mmHg.

Ganoderma lucidum has little or no effect on the amplitude of the pulse pressure. The difference produced by different concentrations of *Ganoderma lucidum* (1mg/ml, 10 mg/ml, and 50 mg/ml) is statistically insignificant. On mean arterial blood pressure (MABP), *Ganoderma Lucidum* has a decreasing effect that is statistically significant. For example, the effect produced at volume 0.1 ml of extract dose concentration of 1mg/ml, 10 mg/ml and 50 mg/ml are 25.50 ± 5.00 mmHg, 25.50 ± 4.50 mmHg and 25.50 ± 0.25 mmHg respectively compared to that of normal saline 0.9% w/v, 29.50 ± 0.5 mmHg.

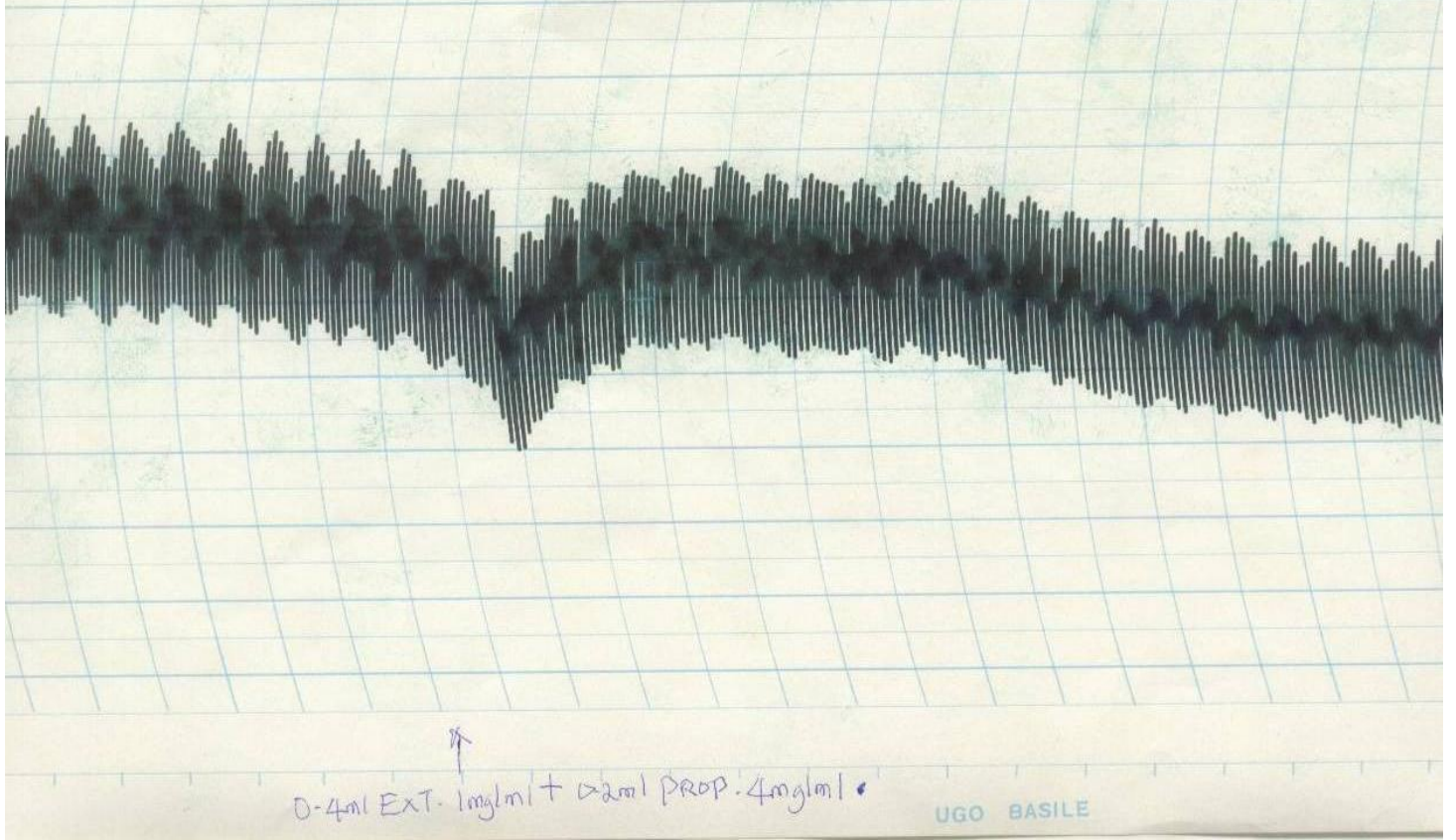
From the table above, the hypotensive effect of 0.8 ml *Ganoderma lucidum* 10 mg/ml is blocked by 0.2 ml atropine 100 μ g/ml. The effects are prominent on the systolic, diastolic and mean arterial blood pressure but not prominent on the pulse pressure. 0.2 ml Propranolol 4 mg/ml partially blocked the activities of the 0.8 ml *Ganoderma lucidum* extract 10 mg/ml, but this is statistically insignificant.

However, the blockade produced by both atropine and Propranolol are said to be statistically insignificant, but the change that occurred with this two drugs are not great enough to exclude the possibility that the difference is due to chance.

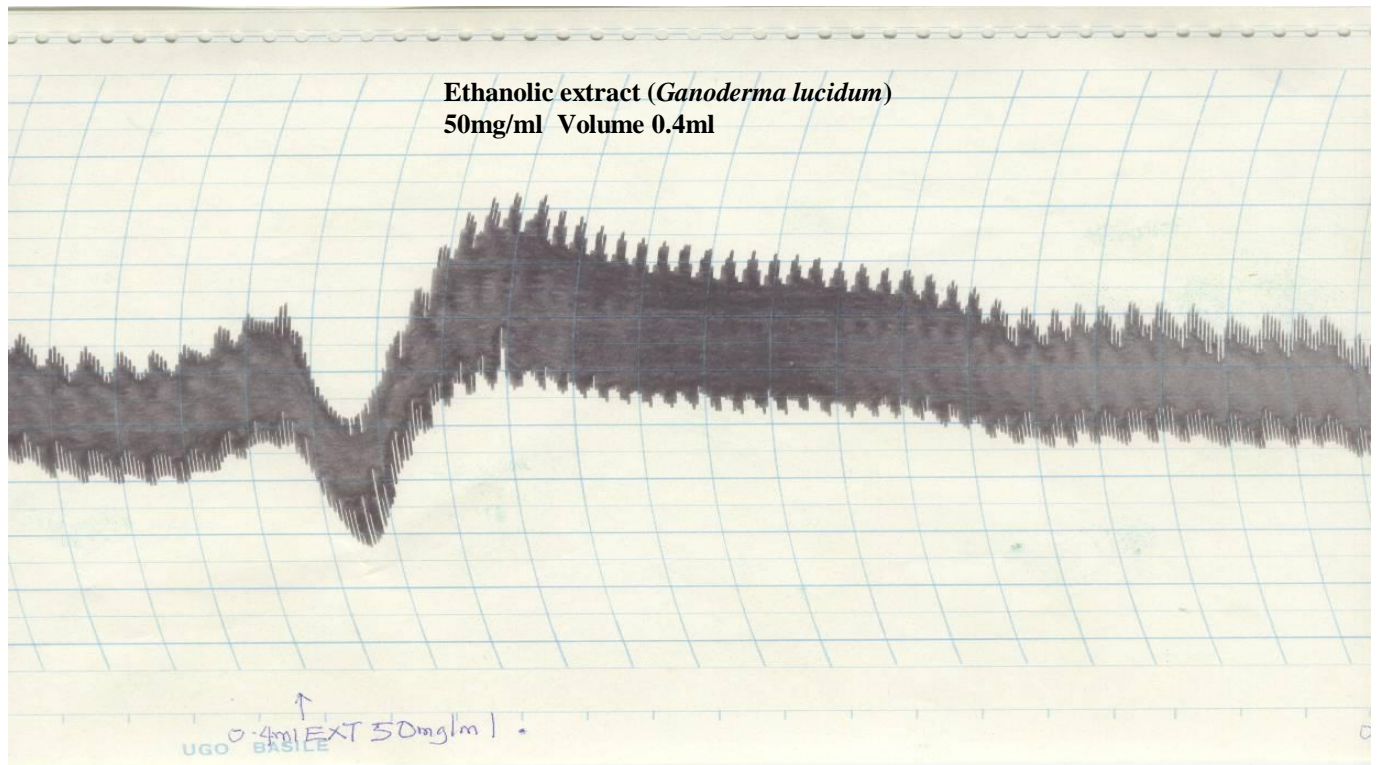
This work is in consonant with the work of Lee et al. (1990) whose work suggests that the mycelium extract from *Ganoderma lucidum* inhibited sympathetic outflow and concluded that this was responsible for the hypotensive effect. Morigwa et al. (1986) demonstrated that a 70% methyl alcohol extract of *Ganoderma lucidum* inhibited angiotensin-converting enzyme. This would limit blood pressure by blocking the rennin-angiotensin. Kabir et al studied the effect of a powder prepared from the culture fruit body of *Ganoderma lucidum* on the blood on the blood pressure of spontaneously hypertensive rat. After a 4-week feeding period, the systolic blood pressures of the rat significantly lower than the control, indicating that the powder contained a substance that suppresses the elevation of blood pressure.

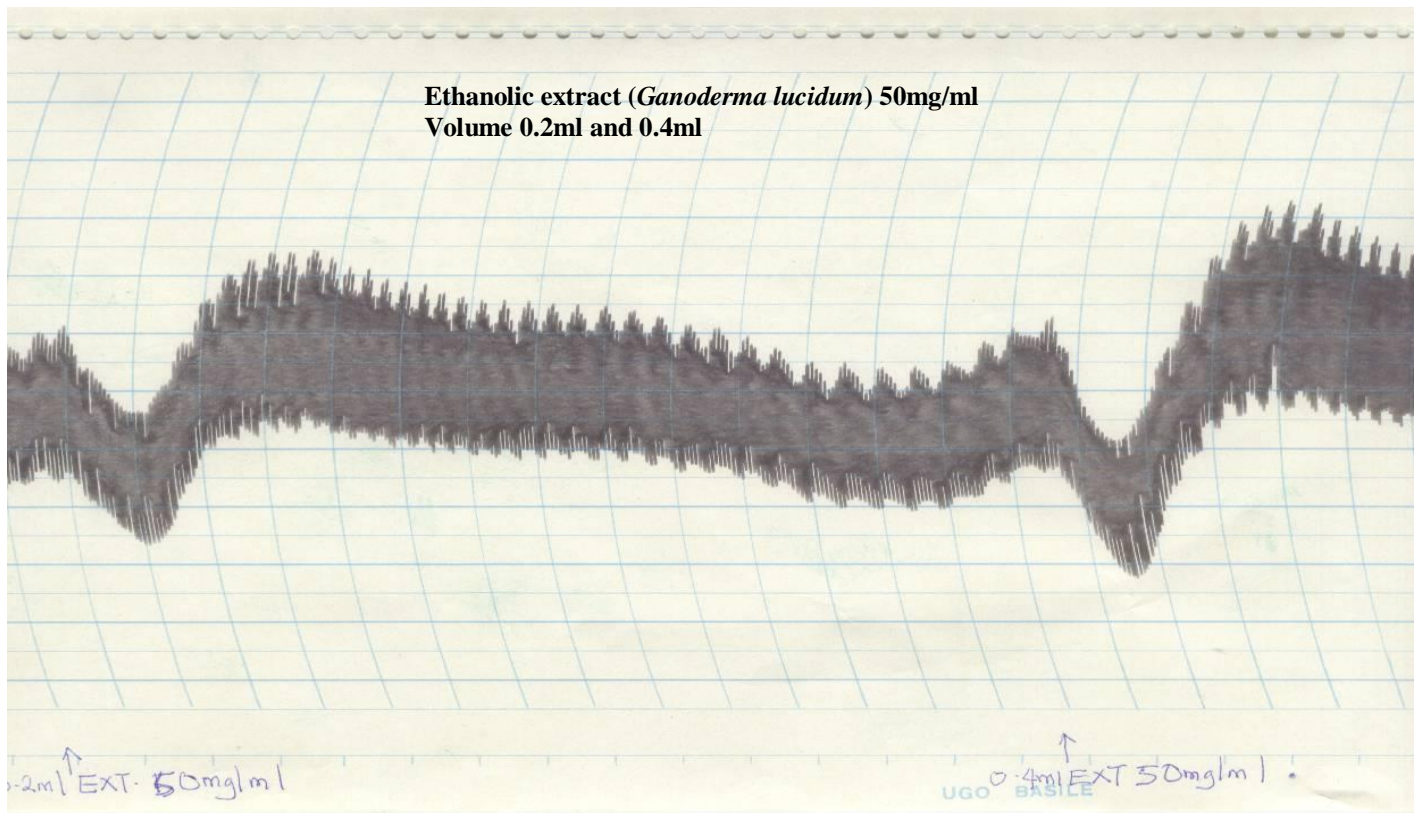
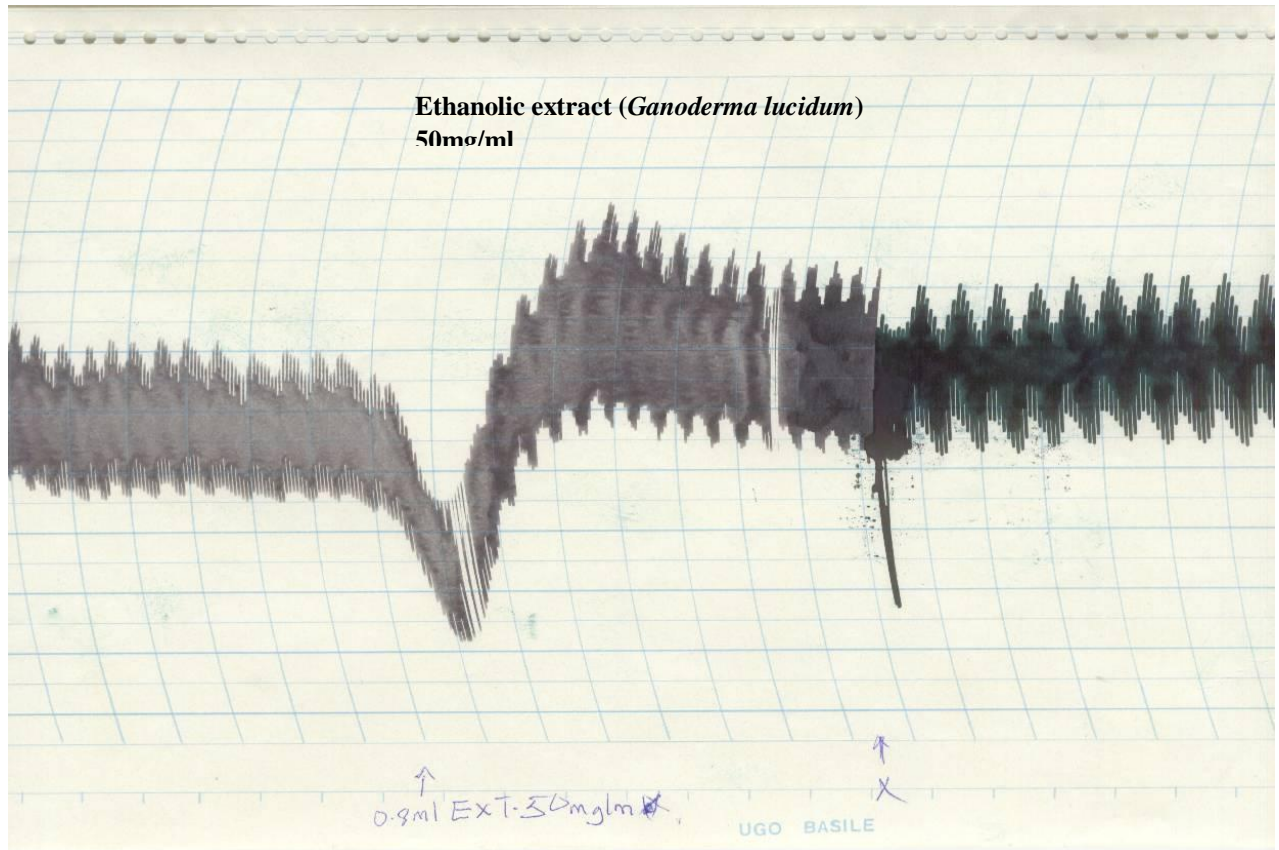


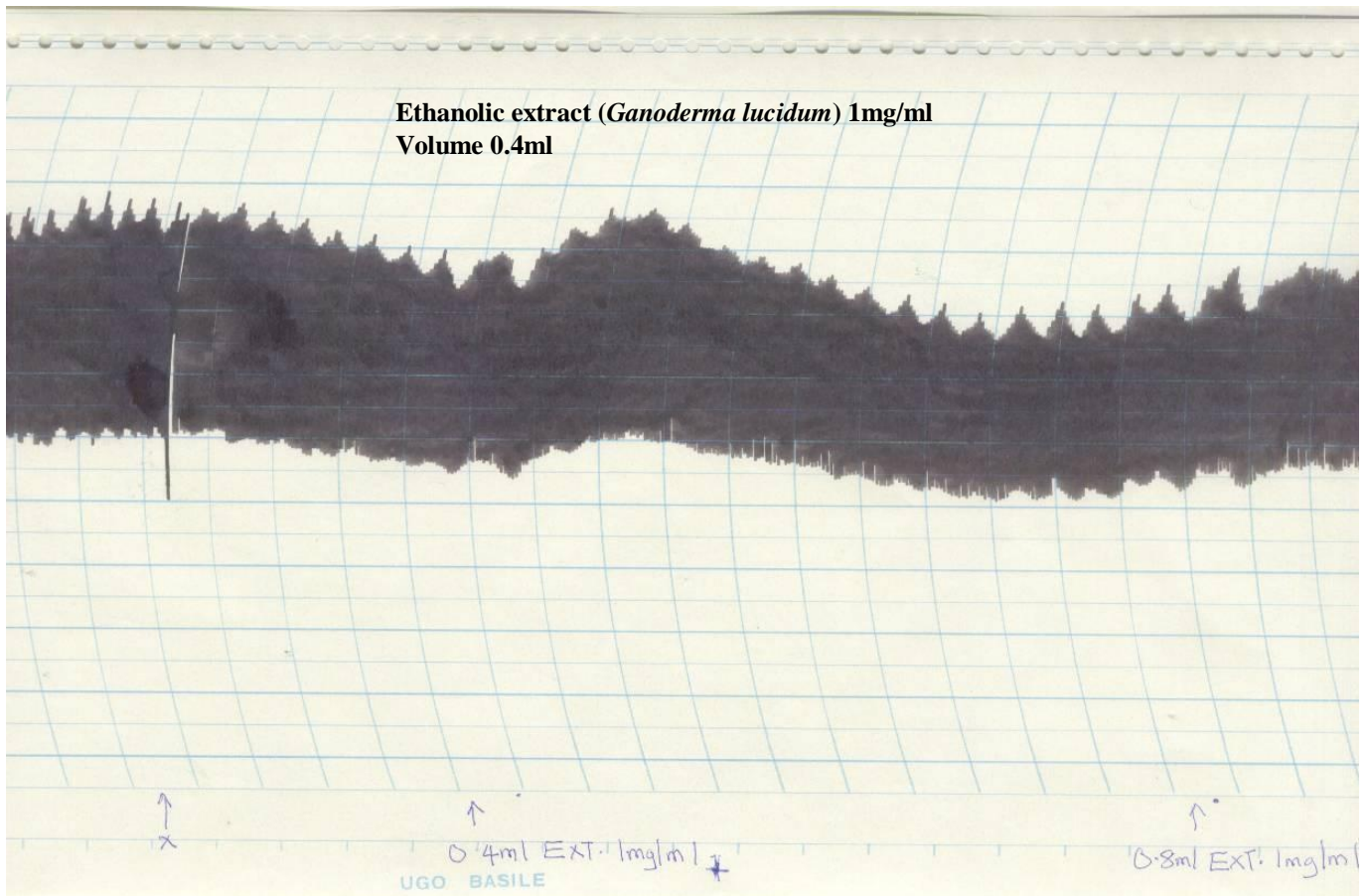
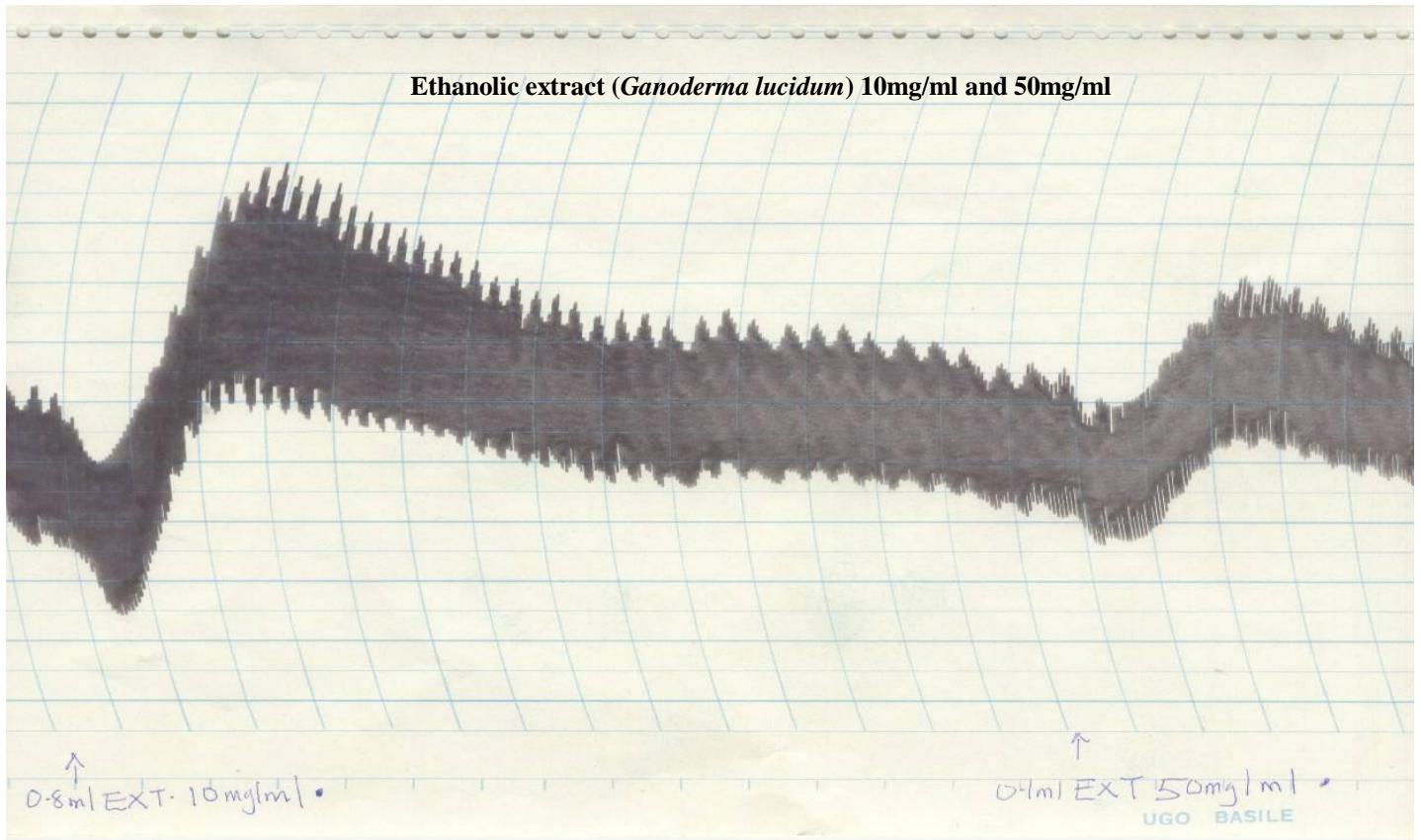
**Drug interaction between Propranolol of 4mg/ml (0.2ml) and
Ethanolic extract (*Ganoderma lucidum*) 1mg/ml (0.4ml)**

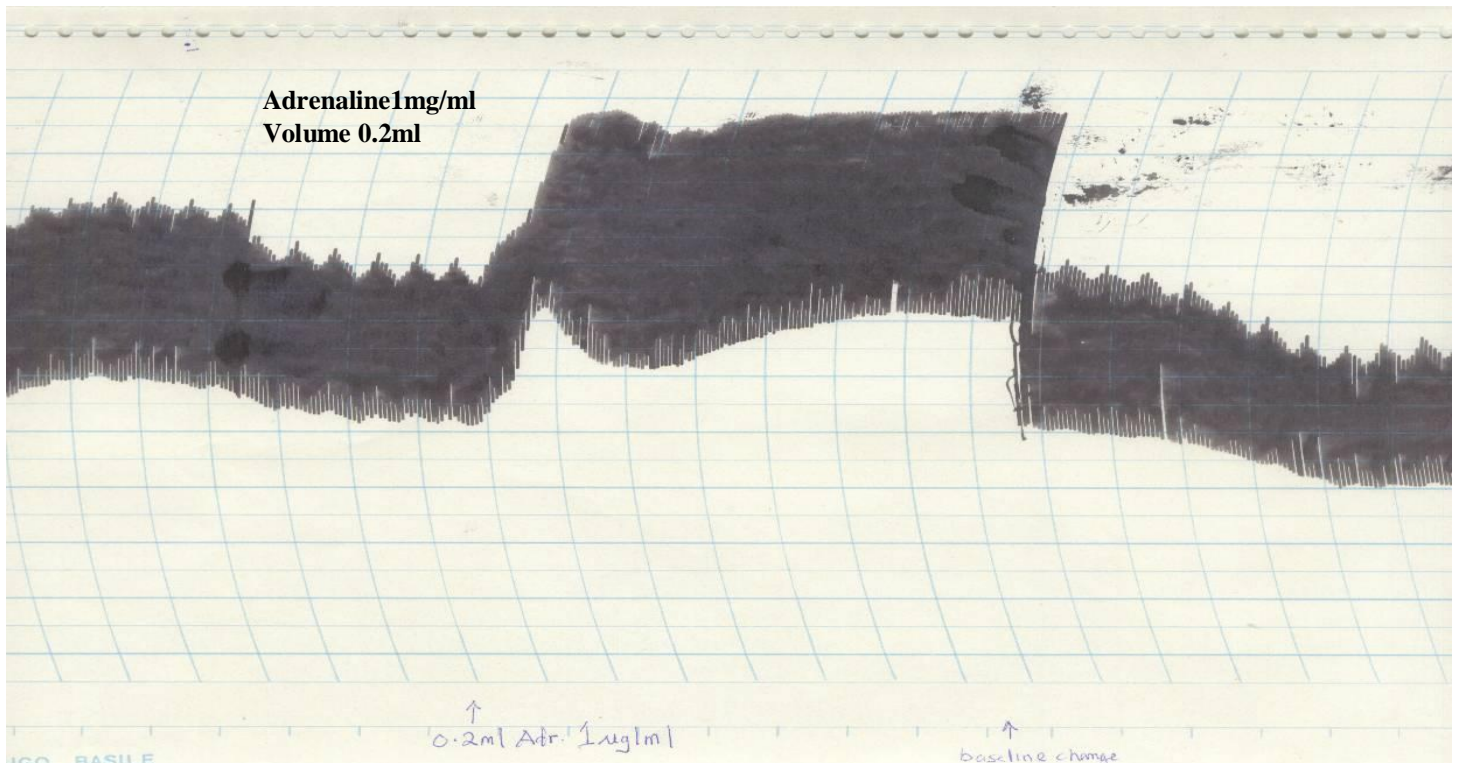
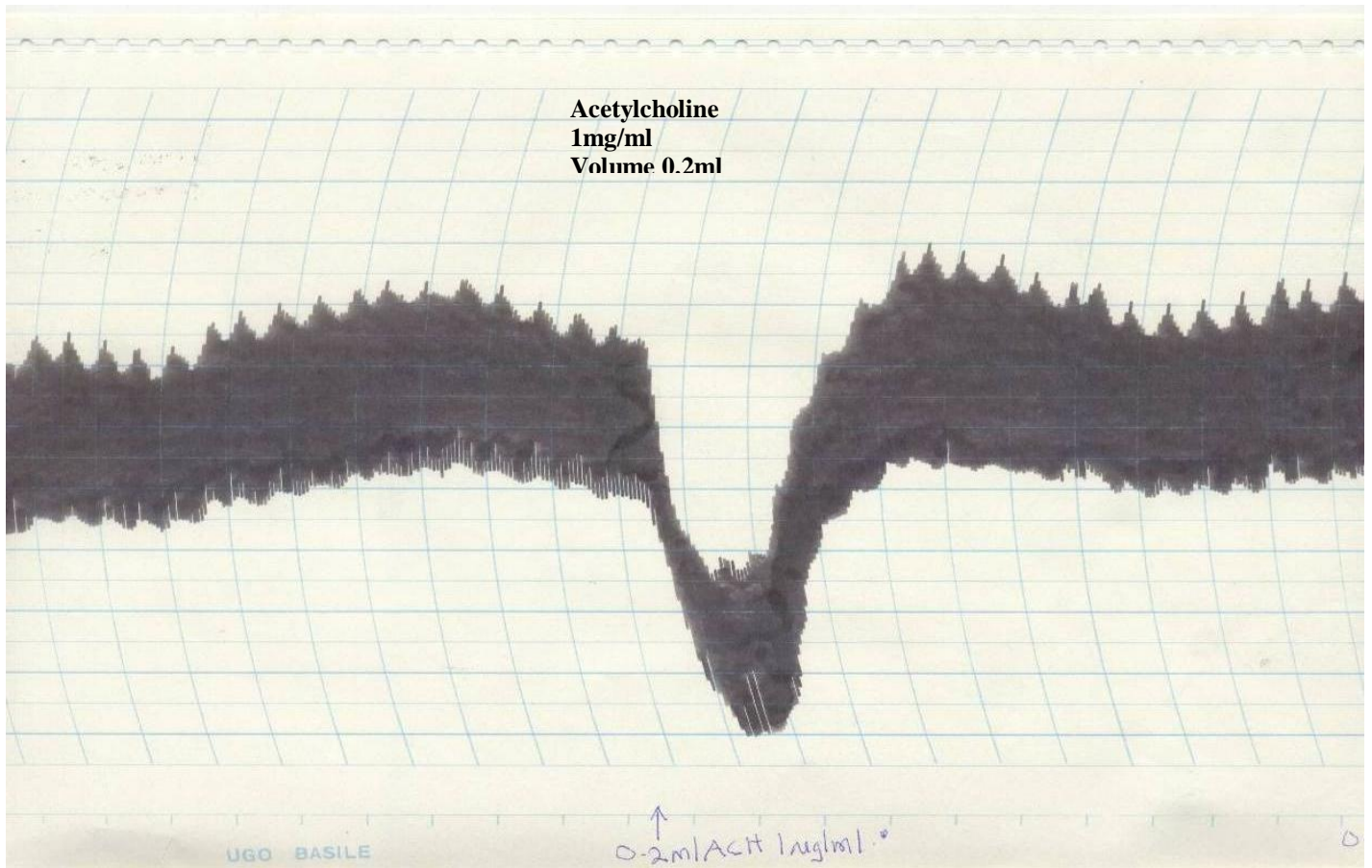


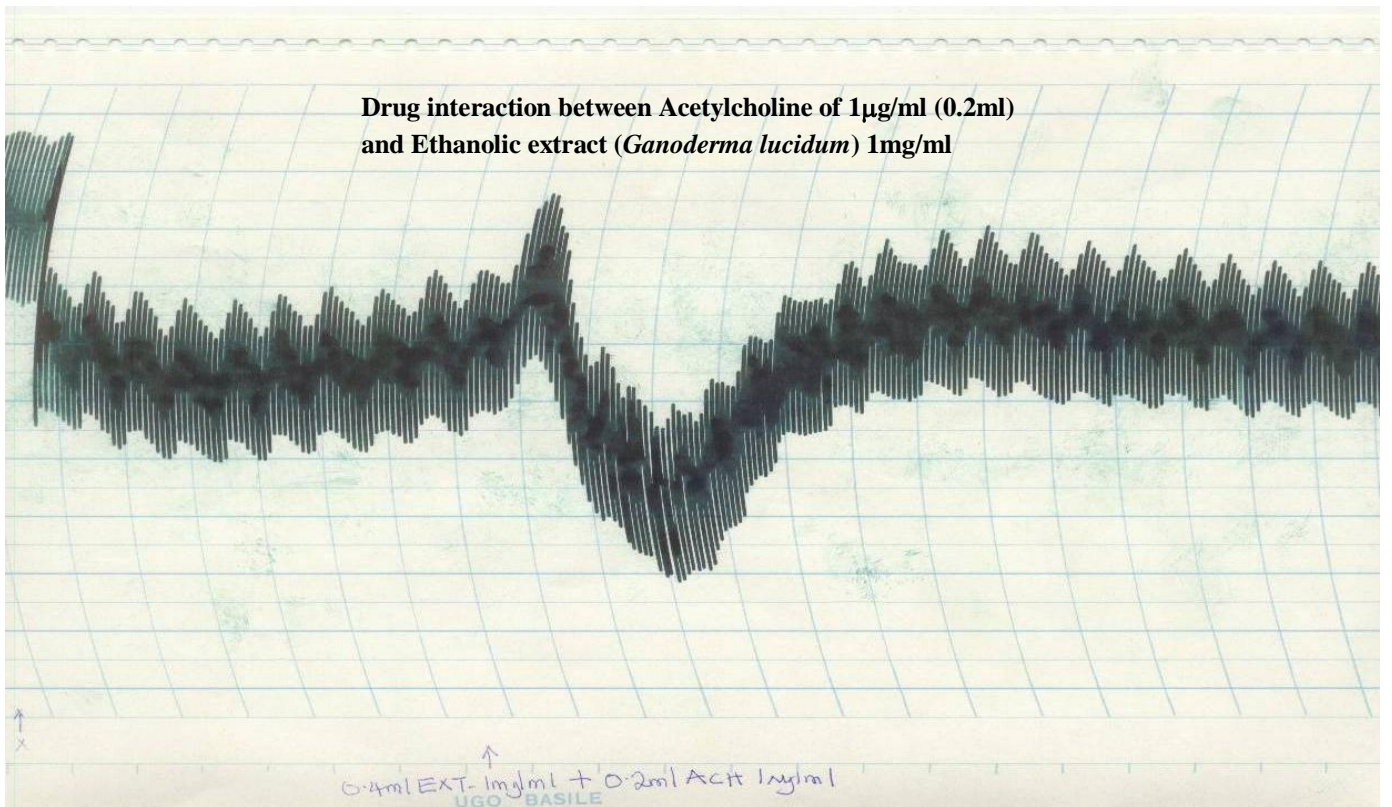
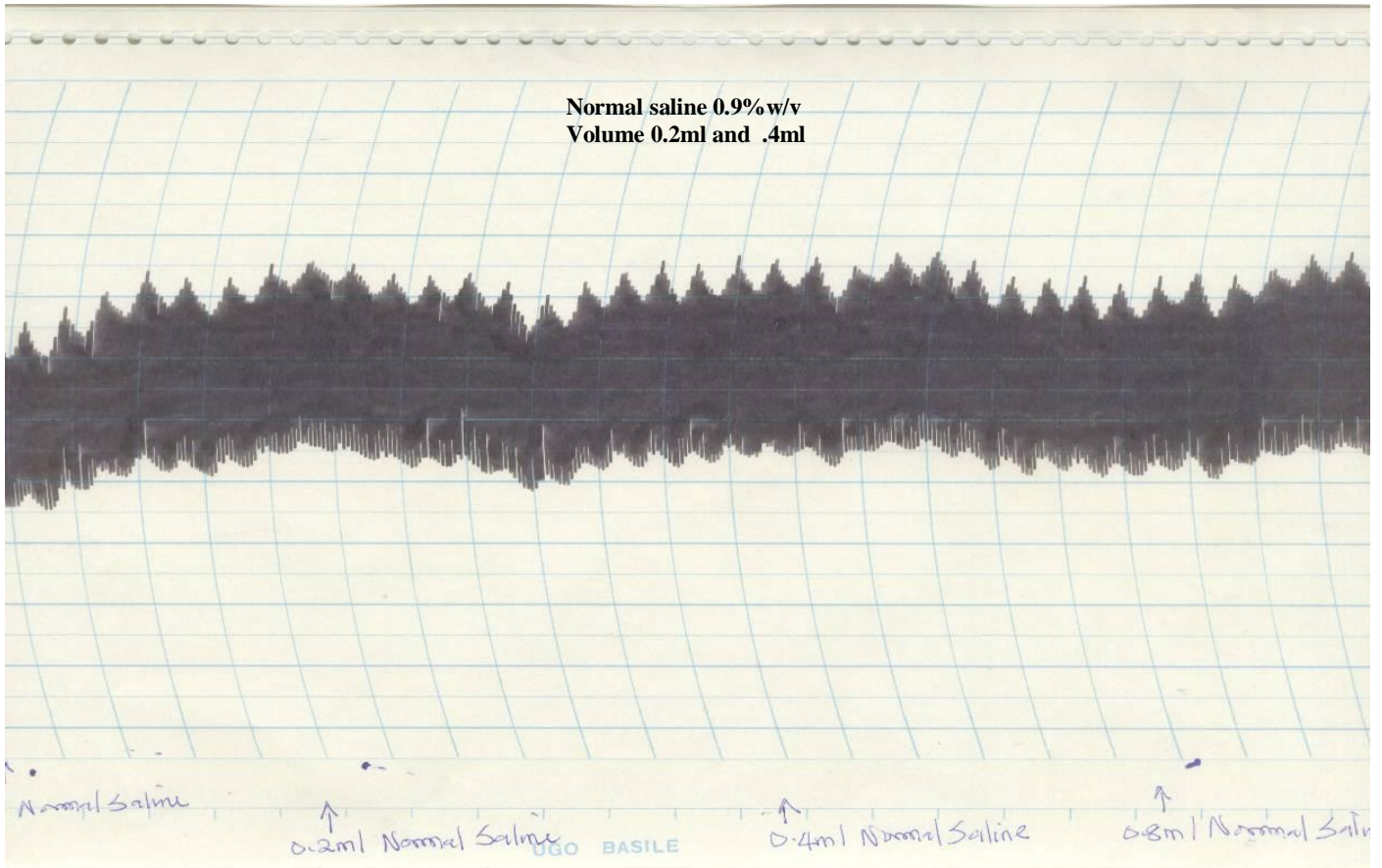
**Ethanolic extract (*Ganoderma lucidum*)
50mg/ml Volume 0.4ml**

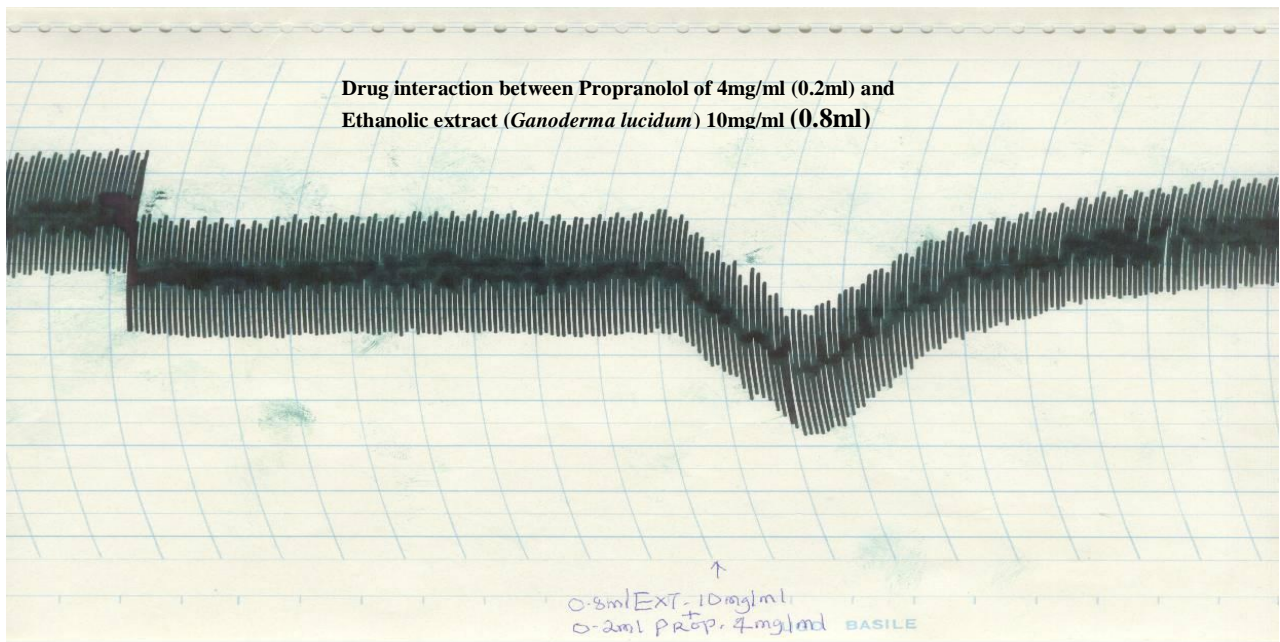
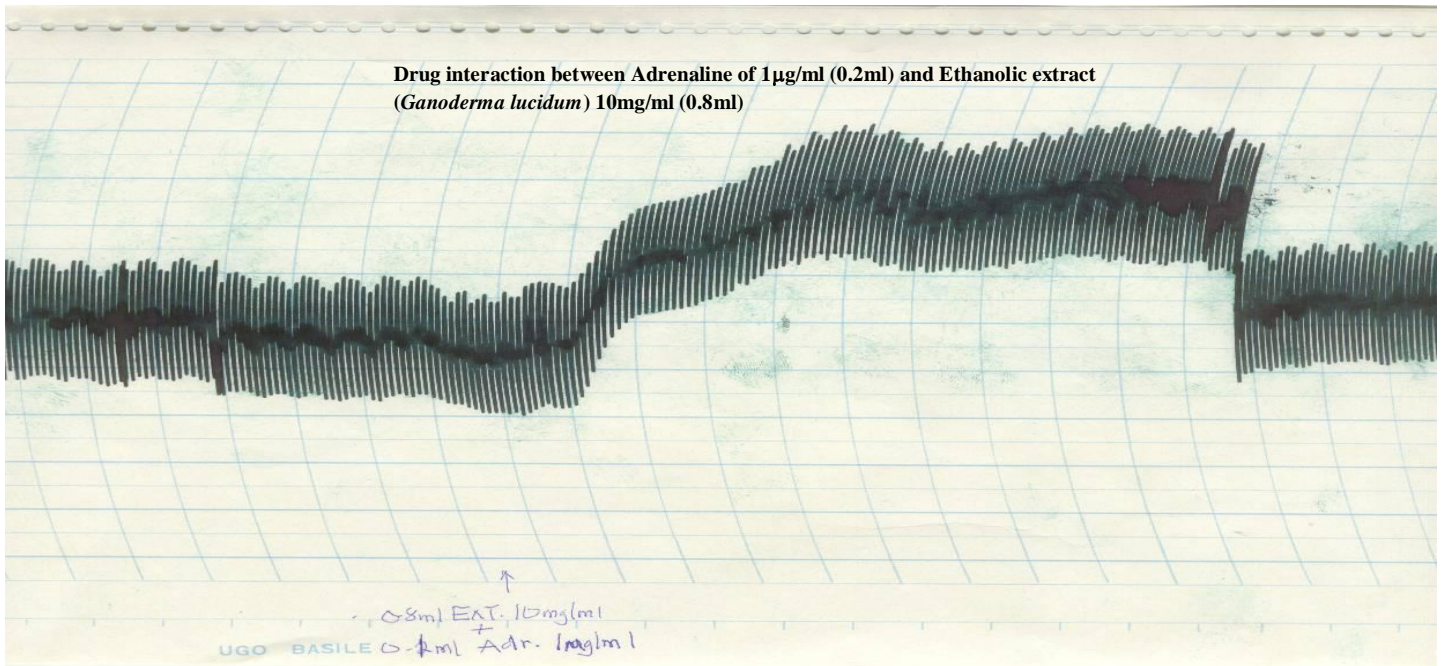


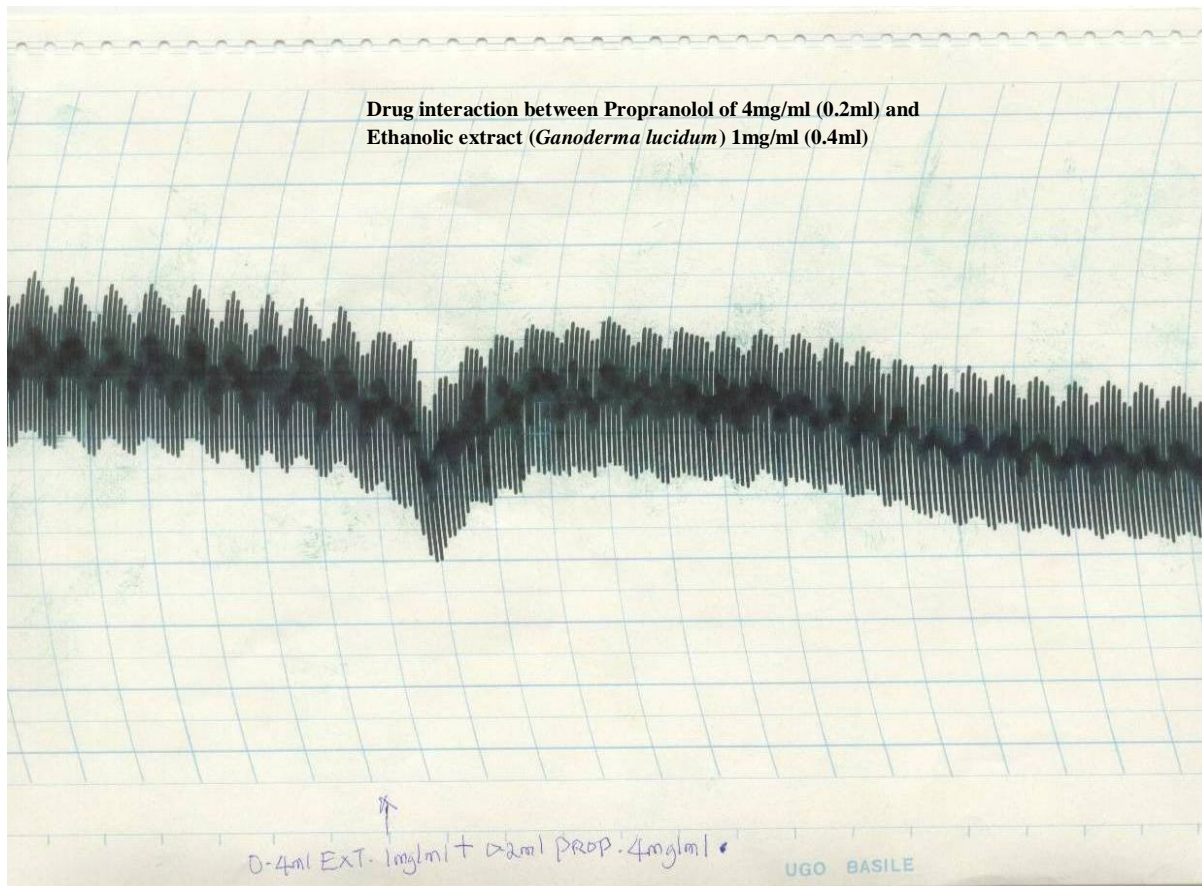
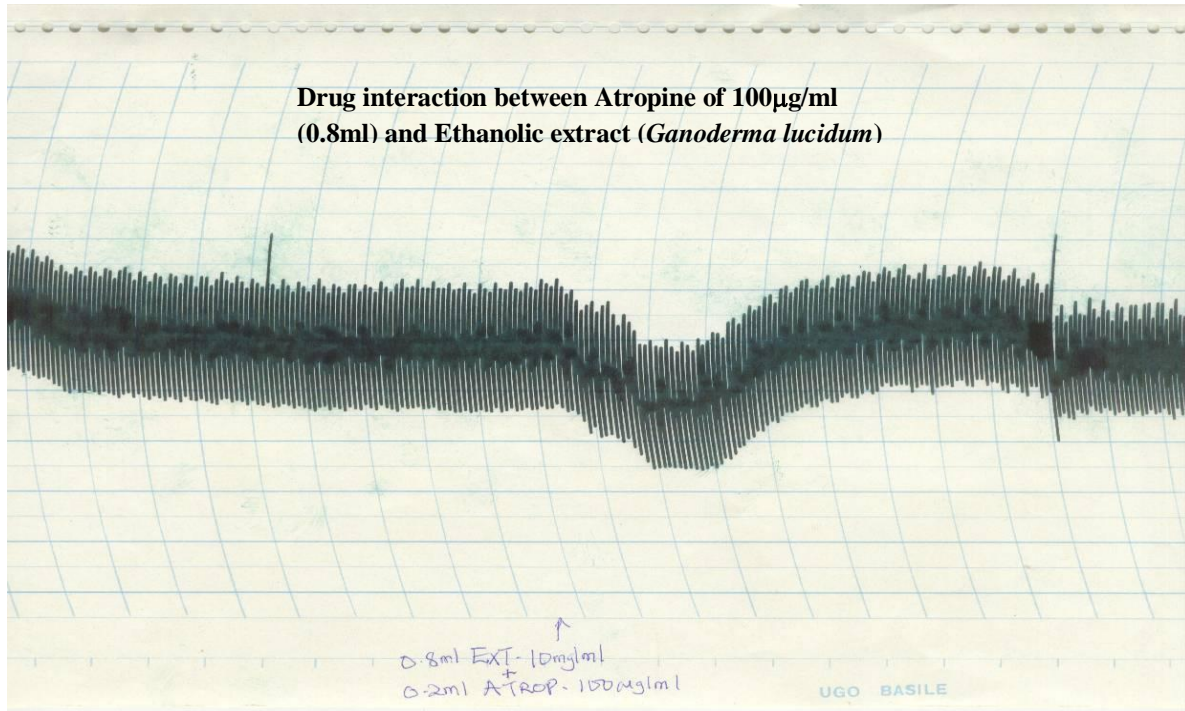












Conclusion:-

The fruiting body ethanol extract of *Ganoderma lucidum* of the Ganodermataceae family was found to have demonstrated a significant ($p < 0.05$) and dose- dependant hypotensive activity at doses of 1,10 and 50ml/kg respectively normal arterial blood pressure in healthy subject.

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