CLINICAL AND HAEMATO-BIOCHEMICAL STUDIES ON PROLONGATION OF PROPOFOL ANAESTHESIA USING ETHER IN DOGS

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Submitted to the

JAWAHARLAL NEHRU KRISHI VISHWA VIDYALAYA, JABALPUR

in partial fulfilment of the requirements for the Degree of

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IN
VETERINARY SURGERY & RADIOLOGY

~: BY :~

RESHMA JAIN

B.V.Sc. & A.H.

DEPARTMENT OF VETERINARY SURGERY & RADIOLOGY
COLLEGE OF VETERINARY SCIENCE AND ANIMAL HUSBANDRY
JAWAHARLAL NEHRU KRISHI VISHWA VIDYALAYA
JABALPUR (M.P.)

2003

DEDICATED TO

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CERTIFICATE-I

This is to certify that the thesis entitled **"CLINICAL AND HAEMATO-BIOCHEMICAL STUDIES ON PROLONGATION OF PROPOFOL ANAESTHESIA USING ETHER IN DOGS"** submitted in partial fulfilment of the requirements for the award of the degree of **"MASTER OF VETERINARY SCIENCE AND ANIMAL HUSBANDRY"** of Jawahar Lal Nehru Krishi Vishwa Vidyalaya, Jabalpur is a record of the bonafide research work carried out by **DR. RESHMA JAIN** under my guidance and supervision. The subject of the thesis has been approved by the Student's Advisory Committee and the Director of Instructions.

No part of the thesis has been submitted for any other degree or diploma (Certificate awarded etc.) or has been published / published part has been fully acknowledged. All the assistance and help received during the course of the investigation have been duly acknowledged by her.

Dr. M.K. Bhargava
Chairman, Advisory Committee

THESIS APPROVED BY THE STUDENT'S ADVISORY COMMITTEE

Chairman : (Dr. M.K. Bhargava) ----------
Member : (Dr. V.P. Chandrapuria) ----------
Member : (Dr. R.G. Agrawal) ----------
Member : (Dr. Mrs. A. Kushwaha) ----------

CERTIFICATE-II

This is to certify that the thesis entitled **"CLINICAL AND HAEMATO-BIOCHEMICAL STUDIES ON PROLONGATION OF PROPOFOL ANAESTHESIA USING ETHER IN DOGS"** submitted by **DR. RESHMA JAIN** to Jawaharlal Nehru Krishi Vishwa Vidyalaya, Jabalpur in partial fulfilment of the requirement for the award of the degree of **"MASTER OF VETERINARY SCIENCE AND ANIMAL HUSBANDRY"** in the Department of Veterinary Surgery and Radiology, College of Veterinary Science and Animal Husbandry, Jabalpur has been approved after evaluation by the External Examiner and by the Student's Advisory Committee after an oral examination on the same.

Place : Jabalpur
Date : 14-10-03

Dr. M.K. Bhargava
Chairman, Advisory Committee

MEMBERS OF THE ADVISORY COMMITTEE

Chairman : (Dr. M.K. Bhargava) ----------
Member : (Dr. V.P. Chandrapuria) ----------
Member : (Dr. R.G. Agrawal) ----------
Member : (Dr. Mrs. A. Kushwaha) ----------

Head/Incharge of the Department ---------- PROFESSOR AND HEAD Department of Veterinary Surgery & Radiology College of Veterinary Science & Animal Husbandry JABALPUR (M. P.) ----------

Director of Instructions ----------

Director of Instruction J.N.Krishi Vishwa Vidyalaya JABALPUR (M.P.)

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Jain

RESHMA JAIN

LIST OF CONTENTS

CHAPTER	TITLE	PAGE No.
I.	**INTRODUCTION**	**1**
II.	**REVIEW OF LITERATURE**	**4**
	❑ ATROPINE SULPHATE	4
	❑ TRIFLUPROMAZINE HYDROCLORIDE	8
	❑ DIAZEPAM	11
	❑ XYLAZINE	17
	❑ PROPOFOL	22
	❑ DIETHYL ETHER	29
III.	**MATERIALS AND METHODS**	**33**
IV.	**RESULTS**	**38**
	❑ CLINICAL STUDIES	38
	Duration of Anaesthesia	38
	Complete Recovery	38
	Dose of Propofol	39
	Dose of Ether	39
	Rectal Temperature	39
	Respiration Rate	39
	Heart Rate	40
	❑ HAEMATOLOGICAL STUDIES	40
	Total Erythrocyte Count (TEC)	40
	Total Leucocyte Count (TLC)	41
	Packed Cell Volume (PCV)	41
	Haemoglobin Concentration (Hb)	42

CHAPTER	TITLE	PAGE No.
	Differential Leucocyte Count (DLC)	42
	❑ BIOCHEMICAL STUDIES	43
	Plasma Glucose	43
	Plasma Protein	44
	Plasma Alanine Amino Transferase	44
	Plasma Alkaline Phosphatase	45
	Plasma Urea Nitrogen	45
	Plasma Creatinine	46
V.	**DISCUSSION**	**47**
VI.	**SUMMARY**	**60**
VII.	**CONCLUSION**	**63**
VIII.	**SUGGESTIONS FOR FURTHER WORK**	**64**
IX.	**REFERENCES**	**65**
	VITA	

LIST OF TABELS

TABLE NO.	TITLE	BETWEEN PAGE
1.	Clinical observations among different treatments in dogs.	38-39
2.	Mean values (±SE) of Rectal Temperature (°F) at different time intervals following three treatments in dogs.	38-39
3.	Mean values (±SE) of Respiration Rate (per minute) at different time intervals following three treatments in dogs.	38-39
4.	Mean values (±SE) of Heart Rate (per minute) at different time intervals following three treatments in dogs.	39-40
5.	Mean values (±SE) of Total Erythrocyte Count (million/cu. mm.) at different time intervals following three treatments in dogs.	39-40
6.	Mean values (±SE) of Total Leucocyte Count (thousand/cu. mm.) at different time intervals following three treatments in dogs.	40-41
7.	Mean values (±SE) of Packed Cell Volume (per cent) at different time intervals following three treatments in dogs.	40-41
8.	Mean values (± SE) of Haemoglobin Concentration (gm per cent) at different time intervals following three treatments in dogs.	41-42
9.	Mean values (±SE) of Neutrophil (per cent) at different time intervals following three treatments in dogs.	41-42
10.	Mean values (±SE) of Eosinophil (per cent) at different time intervals following three treatments in dogs.	41-42
11.	Mean values (±SE) of Monocyte (per cent) at different time intervals following three treatments in dogs.	42-43
12.	Mean values (±SE) of Lymphocyte (per cent) at different time intervals following three treatments in dogs.	42-43
13.	Mean values (±SE) of Plasma Glucose (mg/dl) at different time intervals following three treatments in dogs.	42-43

TABLE NO.	TITLE	BETWEEN PAGE
14.	Mean values (±SE) of Plasma Protein (gm/dl) at different time intervals following three treatments in dogs.	43-44
15.	Mean values (±SE) of Plasma Alanine Amino Transferase (ALT) (IU/liter) at different time intervals following three treatments in dogs.	43-44
16.	Mean values (±SE) of Plasma Alkaline Phosphatase (IU/Liter) at different time intervals following three treatments in dogs.	44-45
17.	Mean values (±SE) of Plasma Urea Nitrogen (mg /dl) at different time intervals following three treatments in dogs.	44-45
18.	Mean values (±SE) of Plasma Creatinine (mg /dl) at different time intervals following three treatments in dogs.	45-46

LIST OF FIGURES

FIGURE NO.	TITLE	BETWEEN PAGE
1.	Duration of anaesthesia and complete recovery after administration of propofol and anaesthetic ether in combination with preanaesthetics in dogs	48-49
2.	Dose of propofol after administration of propofol and anaesthetic ether in combination with preanaesthetics in dogs	49-50
3.	Dose of ether after administration of propofol and anaesthetic ether in combination with preanaesthetics in dogs	49-50
4.	Temperature after administration of propofol and anaesthetic ether in combination with preanaesthetics in dogs	49-50
5.	Respiration rate after administration of propofol and anaesthetic ether in combination with preanaesthetics in dogs	50-51
6.	Heart rate after administration of propofol and anaesthetic ether in combination with preanaesthetics in dogs	51-52
7.	Total erythrocyte count after administration of propofol and anaesthetic ether in combination with preanaesthetics in dogs	52-53
8.	Packed cell volume after administration of propofol and anaesthetic ether in combination with preanaesthetics in dogs	52-53
9.	Haemoglobin concentration after administration of propofol and anaesthetic ether in combination with preanaesthetics in dogs	52-53
10.	Total leucocyte count after administration of propofol and anaesthetic ether in combination with preanaesthetics in dogs	53-54

FIGURE NO.	TITLE	BETWEEN PAGE
11.	Neutrophil count after administration of propofol and anaesthetic ether in combination with preanaesthetics in dogs	53-54
12.	Monocyte count after administration of propofol and anaesthetic ether in combination with preanaesthetics in dogs	53-54
13.	Lymphocye count after administration of propofol and anaesthetic ether in combination with preanaesthetics in dogs	54-55
14.	Eosinophil count after administration of propofol and anaesthetic ether in combination with preanaesthetics in dogs	54-55
15.	Plasma glucose after administration of propofol and anaesthetic ether in combination with preanaesthetics in dogs	55-56
16.	Plasma protein after administration of propofol and anaesthetic ether in combination with preanaesthetics in dogs	56-57
17.	Plasma alanine amino transferase after administration of propofol and anaesthetic ether in combination with preanaesthetics in dogs	57-58
18.	Plasma alkaline phosphatase after administration of propofol and anaesthetic ether in combination with preanaesthetics in dogs	57-58
19.	Plasma urea nitrogen after administration of propofol and anaesthetic ether in combination with preanaesthetics in dogs	58-59
20.	Plasma creatinine after administration of propofol and anaesthetic ether in combination with preanaesthetics in dogs	58-59

~~~ Introduction

INTRODUCTION

Anaesthesia is one of the miracle of the medicine without which modern surgery would have not been possible. Anaesthetic agents are generally depressants, affecting central nervous system and to a lesser extent hepatic and renal functions (Gray and Rees, 1952).

Perfect anaesthesia is "Sine qna non" for successful surgical intervention with objectives to obtain optimum hypnosis, analgesia and muscle relaxation. Selection of appropriate drugs for induction and maintenance, are the main determinants for successful out come of anaesthesia or surgical intervention.

Co-operation of patient in surgical procedures plays an important role and many times untoward movements of patient interfere with the surgical procedure and may lead to serious surgical complication. It is therefore essential to restrain the animal calm and quite, on operation table. Premedicants are used to allay anxiety, calmdown the patient and alicit an anaesthetic adjuvant effect. General anaesthesia was first introduced in animal practice by inhalation of ether. Induction of general anaesthesia directly with inhalant anaesthetics is not practicable in all the circumstances, specially in animals because of struggling during administration of anaesthesia. Induction of anaesthesia with intravenous agents and its maintenance with inhalation anaesthetics has many potential advantages, as the procedure is comparatively easy. This is particularly important in veterinary surgery where trained anaesthetists are not available.

Till now, thiopentone sodium and ketamine are commonly employed general anaesthetic agents in veterinary practice, which are reliable, rapid in action and provide smooth recovery but they do have certain disadvantages. Thiopentone produces vacolization, thrashing and hyperexcitement during recovery (Robinson *et al.*, 1986) and repeated administration have a cumulative effect resulting in to prolonged periods of recovery due to its slow metabolism in body. Ketamine is one of the dissociative general anaesthetic with rapid, non narcotic action. The normal protective reflexes like pharyngeal and laryngeal are maintained and excessive muscle tone is noticed after the administration of ketamine. Ketamine can not be used in intraocular and head injuries due to its stimulatory effect on blood pressure (Lumb and Jones, 1984).

Propofol is a non barbiturate intravenous general anaesthetic that has been recently introduced in veterinary anaesthetic practice. It is a short acting general anaesthetic with rapid onset, quick recovery and lack of cumulative effect even after prolonged administration. The incidence of excitatory side effects during surgery under propofol anaesthesia are low (Watney and Pablo,1992). Recovery from anaesthesia is usually rapid and produces less nausea and vomiting, which are essential requirement during all types of surgery. Briggs *et al.* (1982) compared propofol with thiopentone in human patient and concluded that unlike thiopentone propofol does not increases the sensitivity to somatic pain. Propofol produce anaesthesia of short duration and to prolong the duration of anaesthesia, its repeated or continuos I.V. infusion is required, which increases the cost of anaesthesia in veterinary practice.

Anaesthetic ether is an organic compound commonly used in canine practice. Hall and Clarke (1983) described ether as safer and better

muscle relaxant as compared to other inhalation anaesthetics. Diethyl ether can be easily preserved, less expensive and can be administered with minimum available equipments.

The detail and systematic information regarding the use of propofol along with anaesthetic ether is lacking. Therefore the present experiment was designed to evaluate the efficacy of propofol and anaesthetic ether combination as the general anaesthetic in combination with triflupromazine, xylazine and diazepam as preanaesthetics drugs in dogs with the following objectives:-

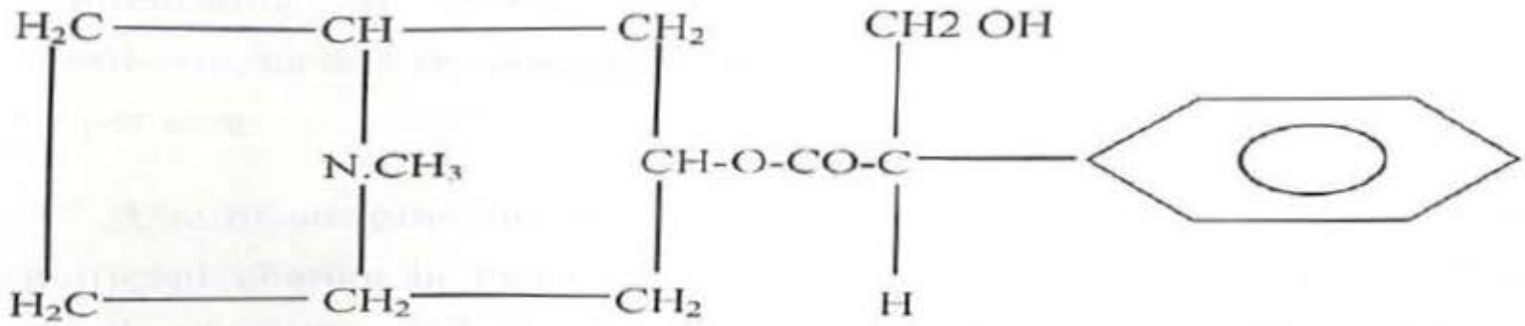
1. To asses the efficacy of propofol and anaesthetic ether as general anaesthetic in combination with different preanaesthetics in dogs.

2. To evaluate the effect of these combinations on different clinical haematological and biochemical parameters in dogs.

~~~ Review of Literature

ATROPINE SULPHATE

Atropine is an alkaloid, extracted from the belladona plant (Solanaceae family) that includes *Atropa belladona* (deadly nightshade), *Datura stramonium* (jimson weed) and *Hyoscyamus niger* (henbane). It is the most commonly used parasympatholytic agent in animal practice (Jones *et al.*, 1977).



Atropine Sulphate

Chemically, atropine is a racemic mixture of 'd' and 'l' hyoscyamine which is an equal mixture of dextro and leo isomer of hyoscyamine. Dextro form of hyoscyamine is biologically inactive. Structurally, atropine molecule consists of two compartments joined together by an ester linkage (i) tropine, an organic base and (ii) tropic acid (Jones *et al.*, 1977).

Clinical studies

Jones (1957) recommended atropine sulphate @ 0.02 mg/lb whereas, Hall and Clarke (1983) suggested its dose @ 0.02 to 0.05 mg/kg

as preanaesthetic for dogs. However, I.V. administration of atropine @ 0.5 mg/kg causes excitement (Hatch, 1967).

Thomas and Woodgate (1966) recommended atropine sulphate as suitable preanaesthetic with the advantage that it corrects the low arterial blood pressure due to reduced heart rate during general anaesthesia.

Hatch (1967) observed that atropine sulphate @ 0.05 mg/kg I.V. reduces the dose of thiopentone sodium by about 2.5 per cent and doubled the period of anaesthesia in dogs. He further recorded that I.V. administration of atropine in dogs recovering from thiopentone anaesthesia, causes re-anaesthetization and increased duration of sleep by 163 per cent.

Use of atropine sulphate alone @ 0.05 mg/kg did not cause any significant change in heart and respiration rate, rectal temperature and arterial pressure. While the premedication with atropine prior to ketamine, acetylpromazine or diazepam-triflupromazine in goats caused an increase in blood pressure, heart and respiration rates (Kumar, 1977).

Kumar *et al.* (1983) reported that atropine premedication accelerates the heart rate due to its parasympathomimetic effect in dogs.

Atropine sulphate was described as a potent anticholinergic which prevented bronchial and salivary secretions (Lumb and Jones, 1984). It helped in preventing vagal preponderence thus able to control possible bradycardia and hypotension (Vickers *et al.*, 1984).

Hsu *et al.* (1985) observed that I.M. injection of atropine sulphate @ 0.045 mg/kg in xylazine premedicated dogs, causes an increase in mean arterial pressure and heart rate. Further, the additional dose (0.01

mg/kg) of atropine sulphate was required to antagonize xylazine induced bradycardia.

Pandey *et al.* (1991) observed significant decrease in temperature, non significant increase in pulse and decrease in respiration rate by using atropine sulphate and diazepam in combination with ketamine in dogs.

Ameerjan *et al.* (1992) induced the anaesthesia with ketamine followed by diazepam in atropinized cats. They suggested that this combination provided good degree of analgesia with quiet and uneventful recovery.

Tiwari *et al.* (1993) used atropine sulphate and morphine sulphate prior to administration of thiopentone (2.5%) or pentobarbitone sodium (2.5%) in dogs and reported decrease in body temperature, respiration and heart rate.

Bisen *et al.* (1994) used pentazocine lactate, buprenorphine or meperidine I.V. after administration of atropine and prior to ketamine anaesthesia in dogs. They recorded significant increase in pulse rate and insignificant decrease in rectal temperature and respiration rate.

Aithal *et al.* (1997) premedicated the dogs with medetomidine (30μ g/kg) and diazepam(1.5mg/kg) and observed significant increase in heart rate, arterial pressure and central venous pressure but non significant decrease in respiration.

Rishniw *et al.* (1999) assesed the effect of different doses (0.04 or 0.06 mg/kg) of atropine in dogs and observed increased heart rate and complete parasympathetic blockade in large breeds of dogs.

Bhatt *et al.* (2001) observed significant decrease in heart rate by using atropine sulpate, medetomidine-ketamine anaeathesia in dogs.

Haemato-biochemical studies

Robinson (1954) observed delayed glucose metabolism after administration of atropine sulphate (300mg) in goats.

Demoor (1968) recorded significant decrease in packed cell volume in horses after administration of atropine sulphate @ 6 mg/100 kg I.M. He further observed that atropine did not caused any change in blood glucose level and arterial acid base status.

Mehta (1971) administered atropine sulphate alone or in combination with diazepam in man and observed significant decrease in blood sugar level.

Kumar and Thurman (1977) reported slight decrease in total erythrocyte count, packed cell volume and haemoglobin concentration 30 minutes after the administration of diazepam in atropinised goats. They further suggested relative lymphocytopaenia and neutrophilia but the values returned to near preadministration levels in 24 to 72 hours.

Pandey *et al.* (1991) used atropine sulphate (0.65 mg /10kg I.V.) and diazepam (3 mg /kg I.V.) as preanaesthetics followed by ketamine (10mg/kg I.V.) in canine surgical patients and reported significant increase in total leucocyte and neutrophil count.

Rajankutty and Nayar (1998) used atropine @ 0.04 mg/kg followed by tilatamine- zolazepam combination in dogs. Decrease in erythrocyte sedimentation rate, packed cell volume, total erythrocyte count,

haemoglobin and lymphocytes and increase in total leucocyte count, neutrophil, serum aspartate aminotransferase (AST), serum alanine aminotransferase (ALT) and blood glucose were seen.

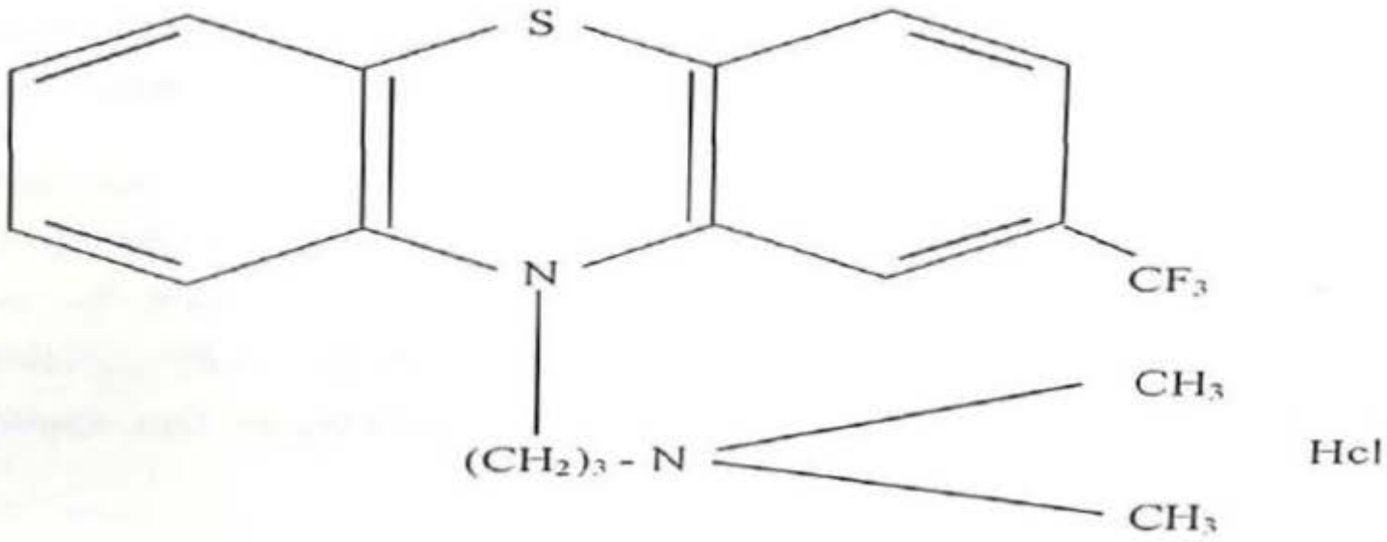
Vishwakarma (2000) recorded significant increase in respiration and pulse rate, where as, non significant decrease in rectal temperature by using midazolam and ketamine in atropinised dogs.

Sharma *et al.* (2002) evaluated the efficacy of triflupromazine with propofol general aneasthesia and observed non-significant increase in blood glucose, serum alkaline phosphatase and blood urea nitrogen, while decrease in serum protein, packed cell volume, lymphocyte, eosinophil and monocyte count.

TRIFLUPROMAZINE HYDROCHLORIDE

Triflupromazine hydrochloride is chemically (2-trifluoromethyl-10-3[3-dimethylamino] propyl) phenothiazine in the hydrochloride salt form. It is available for parenteral use in the dog, cat, cattle and horses. Triflupromazine is designated as tranquilizer or ataractics due to its calming effect. It also posses antiemetic effect but had no analgesic activity though it, decreases the threshold for pain by lowering the alertness.

Triflupromazine depresses the central nervous system by acting at sub cortical level, probably on the brain stem arousal mechanism.



Triflupromazine Hydrochloride

Clinical studies

Jha *et al.* (1961) administered triflupromazine @ 0.5 mg /lb in goats and observed decrease in respiration rate and blood pressure, while increase in heart rate.

Gill *et al.* (1983) used triflupromzine hydrochloride @ 2 mg/kg I.V. as sedative prior to administration of bupivacaine in different doses in dogs and observed non significant changes in the values of temperature, respiration and pulse rates.

Lees (1991) suggested that triflupromazine decreases the body temperature due to increased heat loss through dilated cutaneous blood vessels and effect on hypothalamus.

Ranganath *et al.* (1992) evaluated the effect of buprenorphine-triflupromazine- barbiturate anaesthetic combination in dogs. They observed significant decrease in respiration and temperature but

significant increase in heart rate. These combinations produced optimal sedation, analgesia and muscular relaxation.

Niranjan *et al.* (1994) used ketamine alone and in combination with triflupromazine, chlorpromazine and promazine in cats and recorded duration of anaesthesia as 20-35, 35-60, 40-62 and 16-22 minutes respectively. They further reported insignificant decrease in rectal temperature and respiration rate, whereas, significant increase in heart rate.

Pratap *et al.* (1997) used triflupromazine hydrochloride (1mg/kg), diazepam (1mg/kg), pentazocine lactate (3 mg/kg) and medetomindine (10ugm/kg I.M.) as preanaesthetic in goats and observed increase in respiration and heart rates, whereas, non significant change in rectal temperature.

Sharma *et al.* (2001) used triflupromazine in combination with propofol general anaesthesia in dogs and observed significant increase in heart rate with significant decrease in rectal temperature and respiration rate.

Haemato-biochemical studies

Pandey *et al.* (1982) reported that administration of triflupromazine with glyceryl guaiacolate, thiopentone or chloral hydrate did not produce any significant variations on certain kidney function tests in calves.

Balagopalan *et al.* (1992) assesed the effect of glyceryl guaiacolate alone and in combination with triflupromazine hydrochloride and thiopentone in goats. They observed significant decrease in heart and pulse rates, total erythrocyte and leucocyte counts, haemoglobin, packed

cell volume, systolic and diastolic pressure, mean arterial pressure, lymphocyte count and rectal temperature and non significant decrease in respiration rate. Significant increase in blood glucose was also observed.

David (1993) evaluated efficacy of propofol alone and in combination with triflupromazine hydrochloride in dogs and reported non significant changes in haemotological and biochemical parameters except an increase in blood glucose level during anaesthesia.

Raj *et al.* (1998) administered atropine and triflupromazine hydrochloride followed by lignocaine and pethidine as epidural prior to injection of 2.5% thiopentone sodium I.V. in dogs. They reported increase in total leucocyte count, glucose and cortisol and decrease in cholesterol.

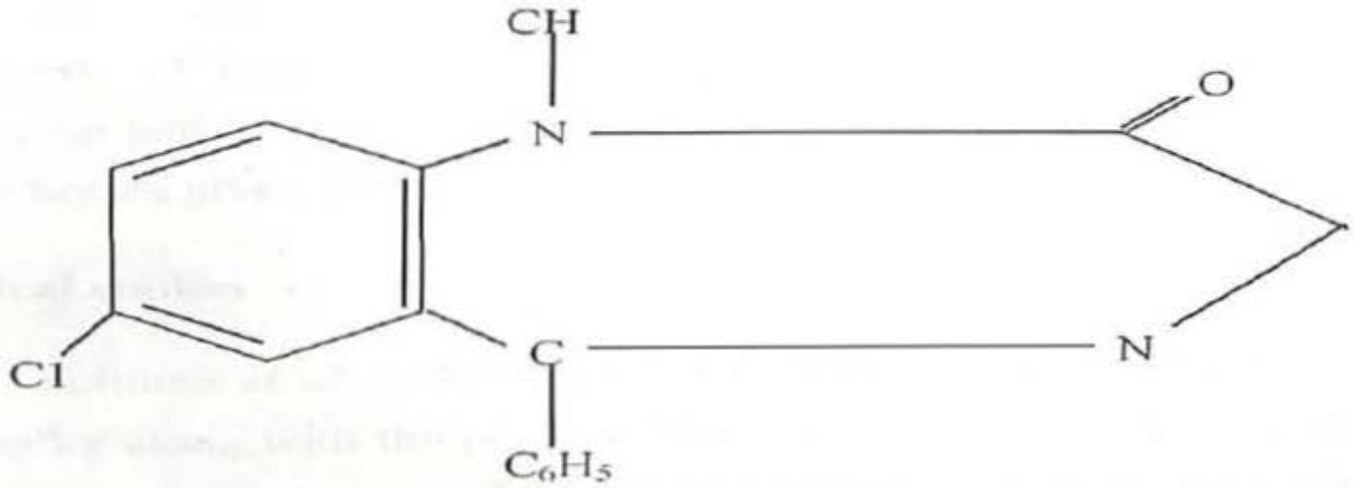
Sharma *et al.* (2002) evaluated the efficacy of triflupromazine as preanaesthetic with propofol and observed non significant increase in blood glucose, serum alkaline phosphatase, blood urea nitrogen while decrease in serum protein, packed cell volume, lymphocyte, eosinophil and monocyte count.

DIAZEPAM

Diazepam (7-Chloro-1, 3- dihydro -1 - methyl - 5- phenyl - 2H -1,4 benzodiazepine-2-1), a benzodiazepine compound, is a white crystalline powder, insoluble in water. The solutions for injection contains solvents such as propylene glycol, ethanol and sodium benzoate in benzoic acid.

It was initially synthesized by Sternbach in Poland in 1933. It is mainly used as a feed additive in domestic animals for its tranquilizing, antistress and growth stimulating effect. It is 10 times more active than

meprobamate in its calming, muscle relaxant and anticonvulsant activities in animals but has no antiemetic activity (Lumb and Jones, 1984).



Diazepam

It is an excellent preanaesthetic agent and shows dose related tranquilizing, sedative and hypnotic properties. Other useful actions include anticonvulsant activity and ability to produce muscle relaxation. The main site of tranquilizing action is in the limbic system of the brain, particularly the hippocampus, while muscle relaxation is completely independent of sedation and is due to an action at spinal-cord level (Hall and Clarke, 1983). Diazepam also produces an effect on the neuro-muscular synapse which may involve direct muscular depression (Dretchen *et al.*, 1971).

Diazpam is rapidly absorbed when given either I.M. or orally and reaches its peak plasma concentration in about 1 to 3 hours. It is metabolized in liver and the process of metabolism is rapid and exhibits greater tissue distribution in dog than in man. The administration of phenobarbital along with diazepam or chronic exposure to diazepam were reported to enhance the diazepam metabolism (Albanus *et al.*, 1972).

Diazepam gets metabolized by demethylation and hydroxylation in man, dog and rat to N-desmethyl diazepam, 3-hydroxydiazepam and oxazepam. N-desmethyl diazepam was identified following glucuronides hydrolysis of urine in horses given 80 mg of diazepam. In addition oxazepam and N-desmethyl diazepam were also detected in urine of one of the horses given 140 mg diazepam, I.V. (Muir *et al.*, 1982)

Clinical studies

Soliman *et al.* (1966) used diazepam as preanaesthetic agent @ 0.5mg/kg along with thiopentone and xylazine - ketamine anaesthesia in dogs and observed an increase in respiration and heart rate after I.M. administration. Whereas, Stovener and Endersen (1966) observed fall in blood pressure with non significant changes in cardiovascular and respiratory functions by using diazepam @ of 0.2 to 0.6 mg/kg I.V.

Balaci and Andreescu (1973) used diazepam in pig @ 1 to 7 mg/kg I.V. and in cow @ 0.8 to 1.0 mg/kg I.V. and 2 to 2.5 mg/kg I.M. for caeserean section, laparotomy, hysterectomy, ovarectomy and castration. The intravenous injection produced muscular relaxation, sleep and analgesia within 5 minutes, whereas, 65 minutes were required after intramuscular injection to produce similar effects.

Bloor *et al.* (1973) recorded an increase in heart rate and decrease in stroke volume in dogs after injection of diazepam @ 1 mg/kg I.V.

Courtol *et al.* (1974) observed slight respiratory depression in sporting horses following I.M. injection of diazepam @ 0.1 mg/kg.

Kumar *et al.* (1983) studied the efficacy of diazepam I.V. as preanaesthetic with barbiturate and observed significant reduction in dose

of barbiturates with quiet and safe induction, adequate muscular relaxation and significantly increased duration of surgical anaesthesia in dogs.

Lumb and Jones (1984) reported that high intravenous dose of diazepam causes slight decrease in respiration, blood pressure, left ventricular stroke work, cardiac output and increase in heart rate.

Bhargava *et al.* (1986) observed a significant increase in the respiration rate and temperature but no significant change in heart rate after I.M. injection of diazepam @ 0.5 mg/kg body weight in male cow calves. Time for appearance and disappearance of drowsiness was 32.71 minutes and 4.58 hours respectively.

Haskins *et al.* (1986) reported that diazepam (0.5 mg/kg) in conjunction with ketamine (10mg/kg) I.V. produces minimum cardiovascular effects, with significant increase in heart rate, marked respiratory depression and less salivation.

Pandey and Sharma (1986) used pentazocine-diazepam combination in canine surgical patients and recorded significant reduction in body temperature and respiration rate, while non significant difference in pulse rate.

Kumar and Singh (1994) observed decrease in onset of effect, duration of surgical anaesthesia and recovery time by using diazepam-ketamine combination in dogs. They also recorded significant decrease in respiration and heart rate and non significant decrease in rectal temperature.

Sharma *et al.* (2001) recorded quicker onset of sedation, good muscle relaxation with diazepam as compared to triflupromazine in neonatal calves.

Aithal *et al.* (2002) used diazepam with halothane in sheep and observed smooth recovery with slight decrease in respiration and transient increase in heart rate.

Haemato-biochemical studies

Solimen *et al.* (1966) observed marked decrease in red blood cells, PCV and Hb concentration with diazepam in dogs.

Girdwood (1976) noticed aplastic anaemia, while Edward (1977) recorded leukocytopenia and leukocytosis in addition to eosinophilia after administration of diazepam in dogs.

Kumar and Thurmon (1977) reported a mild decrease in total red blood cell count, packed cell volume and haemoglobin concentration 30 minutes after the administration of diazepam in goats, whereas lymphocytopenia and neutrophilia were of transient in nature.

A non significant decrease in packed cell volume and haemglobin concentration was reported by Jani *et al.* (1982) during atropine-diazepam-propanidid anaesthesia in dogs, which returned to preanaesthetic level within 48 hours after anaesthesia.

Kumar *et al.* (1985) recorded reduction in packed cell volume and haemoglobin content and significant increase in glucose level in goats anaesthetized with ketamine in combination with diazepam and triflupromazine.

Bhargava *et al.* (1986) used diazepam @ 0.5 mg/kg I.M. in male cow calves and observed significant increase in total erythrocyte count, haemoglobin concentration and packed cell volume.

Pandey and Sharma (1986) did not find any significant change in total erythrocyte count, haemoglobin concentration and erythrocyte sedimentation rate after I.V. administration of diazepam (2 mg/kg) and pentazocine (4 mg/kg). Significant decrease in packed cell volume, total leucocyte count, neutrophil and eosinophil with significant increase in lymphocyte was observed in dogs.

Pandey *et al.* (1991) evaluated the effect of diazepam-ketamine anaesthesia in dogs and recorded significant increase in leucocyte count and neutrophil percentage and significant decrease in lymphocyte percentage.

Chitale *et al.* (1998) observed decrease in PCV, Hb and TEC with neutrophilia and lymphocytopaenia by using diazepam, α - 2 agonist and Ketamine in goats.

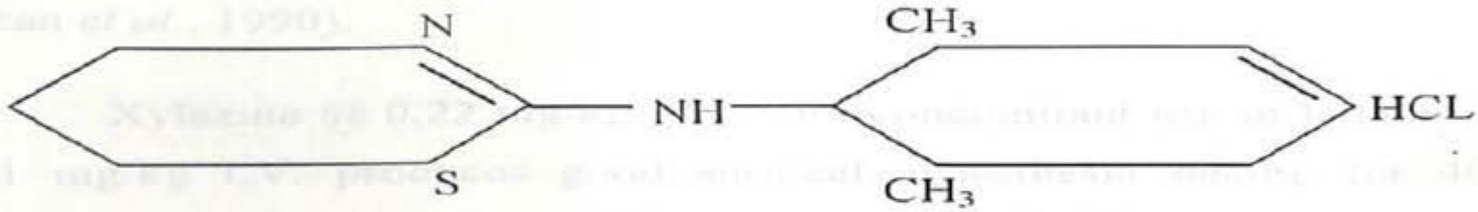
Kandpal and Kumar (1998) used thiopentone with diazepam in calves and observed a non significant decrease in packed cell volume, haemoglobin concentration and total erythrocyte count, with significant increase in blood glucose, urea nitrogen and creatinine.

Gohre *et al.* (1999) studied the effect of epidural administration of diazepam along with lignocaine in dogs and recorded non significant increase in serum protein, AST, ALT and sodium concentration with non significant decrease in serum potassium.

Akhare *et al.* (2000) used diazepam ketamine in goats and noticed non significant decrease in Hb and TEC and significant decrease in PCV and neutrophil count. However, TLC, lymphocyte, eosinophil and monocyte counts were unaffected.

XYLAZINE

Xylazine {2-2,6-di ethylphenylamino 4H-5, 6 dihydro-1,3-thiazine hydrochloride], a potent non narcotic sedative, analgesic and muscle relaxant was first used in Germany (Sanger *et al.* 1968). Since then it has been used successfully in all the domestic and wild animals.



Xylazine hydrochloride

Xylazine produces muscle relaxation by inhibition of intra-neuronal transmission of impulses at the central level of central nervous system. Emesis is commonly induced by xylazine in the cat and occasionally in dogs, because of direct stimulatory effect upon the emetic centre. The pharmacological activity of xylazine in dogs and cattle can be antagonised by 4-aminopyridine and yohimbine hydrochloride (Hatch *et al.* 1982).

Clinical studies

Clarke & Hall (1969) observed that intravenous administration of xylazine @ 0.05 to 1mg/kg produced sleep like state for 1 to 2 hours

duration. Xylazine @ 0.5 mg/kg has been found to produce sedation within 3-5 minutes and 10 to 15 minutes after I.V. and I.M. injections respectively (Lumb and Jones, 1984). The duration of analgesia has also been reported to be directly proportional to the amount of xylazine injected (Khamis and Saleh, 1970).

Increased salivation after xylazine administration has been reported in buffaloes (Peshin and Kumar, 1979) and goats (Kokonen and Eriksson, 1987).

Administration of xylazine produced bradycardia and decrease in respiratory rate in buffaloes (Peshin and Kumar, 1979) and cattle (St. Jean *et al.*, 1990).

Xylazine @ 0.22 mg/kg I.M. with concomitant use of ketamine @ 11 mg/kg I.V. produces good surgical anaesthesia lasting for 40-55 minutes in paediatric patients (Kumar and Singh, 1979).

Sharma et al. (1983) used xylazine and atropine sulphate as preanaesthetics followed by thiopental sodium in dogs and reported decrease in heart and respiration rates, mean arterial blood pressure and body temperature.

Kumar and Singh (1994) observed a significant decrease in respiration and heart rate 10 minutes after xylazine-diazepam administration with maximum decrease at 30 minutes. They further reported good muscle relexation with moderate depression of palpebral and absence of paedal and cough reflexes.

Rector *et al.* (1996) used xylazine I.M. @ 1 mg/kg in six dogs and found low grade analgesia and sedation of one hour duration with significant decrease in body temperature for 2 to 3 hours.

Xylazine caused a non significant decrease in respiratory rate in cattle (Na geli, 1997) while significant decrease in respiration rate in goats (Kumar and Thurmon, 1979).

Ramaswamy *et al.* (1998) administered atropine (0.04 mg/kg S.C.) and xylazine (2 mg/kg I.M) as preanaesthetic prior to telazol 10 mg/kg I.V. and observed significant increase in heart rate and mean arterial pressure, whereas, non significant decrease in respiration rate.

Jiwan and Inho (1999) observed that premedication with xylazine reduces the dose of propofol and incidences of side effects in dogs. They also reported decrease in heart rate, temperature and respiration rate.

Varshney and Singh (2000) observed sedative and analgesic effects of epidural xylazine (0.1 mg/kg) alone and in combination with lignocaine hydrochloride in donkeys and concluded that this combination increases the duration of analgesia.

Butola (2001) reported that atropine-xylazine-midazolam-ketamine combination induces deep surgical anaesthesia with excellent muscular relaxation, analgesia and abolition of various reflexes in dogs.

Khandekar *et al.* (2001), used xylazine, acepromazine and pentazocine as preanesthetics with propofol anaesthesia. They observed better sedation, shorter induction time, better quality of anaesthesia and muscle relaxation with xylazine in combination with propofol as compared to other pre anesthetics.

Raj and Singh (2001) studied the effect of xylazine and midazolam combination in buffalo calves. They observed that midazolam in combination with xylazine decreases the adverse effects of xylazine on heart rate, mean arterial pressure and central venous pressure and produces quick recovery and excellent degree of analgesia.

Tripathi *et al.* (2001) reported faster recovery from xylazine-ketamine anaesthesia in tigers by the use of yohimbine.

Haemato-biochemical studies

Kumar and Thurmon (1979) reported increase in neutrophil count while decrease in total leucocyte, erythrocyte, lymphocyte counts and haemoglobin in goats after the administration of xylazine. Peshin and Kumar (1983) also reported similar findings in cattle and buffalo.

Sharma et al. (1983) used xylazine and atropine sulphate as preanesthetics followed by thiopental sodium in dogs and observed decrease in total erythrocyte, leucocyte count, haemoglobin, packed cell volume, total serum protein and serum electrolytes (sodium, potassium and chloride), whereas, increase in neutrophil count, blood glucose, blood urea nitrogen and serum transaminases (SGOT and SGPT).

Hyperglycaemia was observed following administration of xylazine in goats (Dehghani *et al.*, 1991) and in cattle and buffalo (Arnemo and Soli, 1993).

Dehghani *et al.*, (1991) reported non significant changes in the values of protein, albumin, calcium, potassium, sodium and chloride in buffalo, caprine and feline after the administration of xylazine.

Chitale *et al.* (1998) used xylazine with diazepam and ketamine in goats and recorded significant hyperglycaemia with no change in cholestrol and serum urea nitrogen. They also observed slight increase in bilirubin level.

Tiwari *et al.* (1998) recorded signficant decrease ($P<0.05$) in lymphocyte count while significant increase in neutrophil count after epidural administration of xylazine or detomidine with or without local anaesthetics in buffaloes. Biochemical parameters like serum glucose and sodium showed a significant increase while potassium and chloride level decreased significantly.

Jiwan and In ho (1999) used xylazine premedication with propofol in dogs and observed significant increase in BUN, total protein and albumin with non significant changes in TLC, TEC, MCV, MCH and MCHC.

Verma *et al.* (1999) used xylazine and centbucridine hychochloride epidurally in calves and observed significant decrease in lymphocyte, while increase in neutrophil and eosinophil count. Significant increase in blood glucose, serum alkaline phosphatase and blood urea nitrogen was also observed.

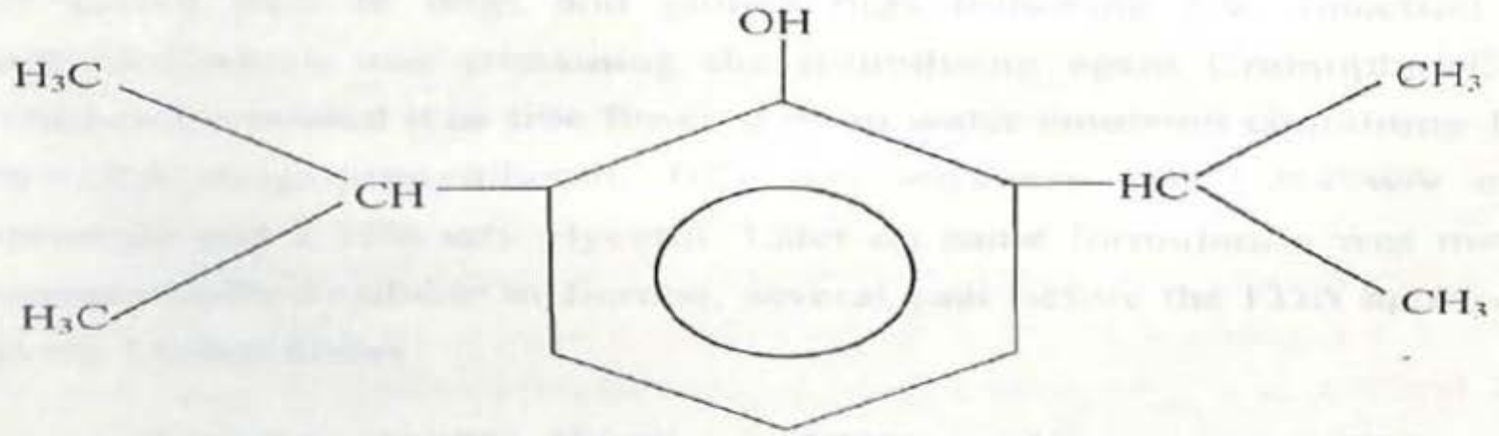
Ameerjan and Gopal (2000) evaluated the effect of xylazine and ketamine on vital organs and recorded non significant changes in kidney liver and brain.

Sooryada (2001) evaluated the effect of xylazine-propofol combination for elective and emergency surgery of dogs and reported significant decrease in haemoglobin and total erythrocyte count.

Shrestha *et al.* (2002) recorded significant increase in total leucocyte and neutrophil with decrease in lymphocyte count after subarachnoid injection of centbucridine in combination with xylazine in goats. Significant increase in blood glucose and serum protein was also observed.

PROPOFOL

Propofol (2,6-di-isopropy1 phenol) is a short acting general anaesthetic with a rapid onset of action of approximately 30 seconds. Recovery from anaesthesia is usually rapid. The mechanism of action, like all other general anaesthetics is poorly understood. The maintenance of anaesthesia with propofol can be achieved by either continuos infusion or intermittent injections. It is white, oil in water, isotonic emulsion for intravenous injection of the drug containing 10 mg propofol per mililiter. The vehicle contains glycerol, purified egg lecithine, sodium hydroxide, soyabean oil and water.



Propofol

Prpofol is extensively distributed and rapidly eliminated from the body (total body clearance 1.5-2 litres/minutes). Clearance occurs by

metabolic process mainly in the liver to form inactive conjugates of propofol and its corresponding quinol, which are excreted in urine.

Propofol was developed following a series of investigations at the department of Clinical Research at ICI. The first clinical trials on propofol were conducted in Belgium.Its brand name was based on the sequence DI-ISOPROPYLPHENOL (Kay and Rolly, 1977).

Clinical studies

James and Glen (1980) reported that propofol had anaesthetic properties in animals and can produce anaesthesia of short duration in small experimental animals. Glen (1980) further studied the different properties of propofol and observed that the drug had limited solubility in aqueous solution. He used this solution for producing anaesthesia in man and laboratory animals with rapid onset, without excitatory side effect.

Glen and Hunter (1984) observed anaphylactic reaction and signs of severe pain in dogs and guinea pigs following I.V. injection of propofol which was containing the solubilising agent Cremophor-E.L. They reformulated it as free flowing oil in water emulsion containing 1% w/v 2,6 di-iso-propylphenol, 10% w/v soyabean oil, 1.2% w/v egg lecithine and 2.25% w/v glycerol. Later on same formulation was made commercially available in Europe, several year before the FDA approval in the United States.

Youngberg (1986), Henrikson (1987) and Vinik *et al.*, (1987) in a comparative study observed that propofol @ 2-2.5 mg/kg was as effective as thiopentone @ 4-5 mg/kg with better recovery.

Hall and Chambers (1987) reported propofol as one of the best induction agent in dogs to produced quite and rapid anaesthesia with smooth and faster recovery.

Watkins *et al.* (1987) observed smooth and excitement free recovery with propofol (5.95 mg/kg body weight) in unpremedicated dogs. The respiratory depression noticed during the course of anaesthesia was also non significant.

Brearley *et al.* (1988) reported that decrease in heart rate after induction with propofol was due to decreased sympathetic stimulation rather than any direct cardiac depressing effects of the drug in cats.

Genevois *et al.* (1988) used propofol at the rate of 8 mg/kg as a single I.V. injection for brief anaesthesia of 4 to 7 minutes in dogs. They further reported that quality of analgesia and muscle relaxation was excellent and the animals stood up and walked normally within an average period of 40 minutes.

Langley and Heel (1988) used it as a hypnotic agent and reported that its distribution in the body was very rapid and converted into inactive metabolites resulting into quick recovery without cumulative effects.

Morgan and Legge (1989) recorded induction doses of propofol for unpremedicated and premedicated dogs as 6.55 mg/kg and 4.5 mg/kg respectively. The effective anaesthesia ranged between 2.5 to 3.8 and 2.5 to 9.4 minutes followed by complete recovery in 24.0±10.0 and 40.0±17.0 minutes respectively.

Flecknell *et al.* (1990) obtained prolonged period of surgical anaesthesia induced with propofol (6.5±1.3 mg/kg) and maintained with continuous infusion at the rate of 0.14 to 0.18 mg/kg/ min in dogs.

Weaver and Reptopoulos (1990) recorded mean induction dose of propofol as 5.2±2.3 mg/kg and 3.6±1.4 mg/kg and recovery from anaesthesia in 16.4±9.0 minutes and 40.4±26.7 minutes in unpremedicated and premedicated dogs respectively. They also observed no change in respiration rate. However, heart, systolic and diastolic blood pressure increased with time.

Vescae and Lucisano (1991) observed that propofol had a shorter half life in goats. They suggested that propofol is a less potent analgesic in this species. On the contrary Reid *et al.* (1993) administered propofol @ 4 mg/kg for induction of anaesthesia prior to maintenance with halothane in goats and observed rapid and smooth induction. They concluded propofol as a very satisfactory anaesthetic agent in this species.

Komar *et al.* (1992) studied the haemodynamic effects of propofol in dogs and observed tachycardia and decreased arterial pressure without any change in cardiac output.

David (1993) studied efficacy of propofol alone and in combination with triflupromazine hydrochloride in dogs. The mean induction dose required for the unpremedicated group was 5.55 mg/kg and for premedicated group 5.2 mg/kg. Significant increase in the heart and pulse rates and decrease in respiratory rate, central venous pressure, blood pressure, pulmonary arterial pressure and body temperature was observed.

Nolan and Reid (1993) observed smooth and rapid induction of anaesthesia with propofol (4mg/kg) following premedication with acepromazine in dogs. They further recorded rapid recovery with mean value of 7.6 minutes and unassisted standing in 30.7 minutes.

Reid and Nolan (1993) studied the pharmacokinetics of propofol in dogs premedicted with acepromazine and maintained with halothane and nitrous oxide. They concluded that propofol was widely distributed and rapidly cleared form the body.

Thurmon *et al.* (1995) administered propofol in two different dose rates viz. 2 mg/kg and 4 mg/kg b. wt. in dogs. Rapid and smooth recovery without any significant changes in the heart rate, respiration rate, mean blood pressure and rectal temperature were recorded in both the groups.

England *et al.* (1996) used four different doses of romifidine (20,40,80 and 120 mg/kg b. wt.) with propofol anaesthesia in dogs and observed non significant changes in respiration, heart rate and rectal temperature.

Gill *et al.* (1996) studied the effect of propofol (@ 4.10 ± 0.75 mg/kg b.wt) after preanaesthetic medication with acepromazine, meperidine and atropine sulphate in dogs. They recorded smooth recovery with no change in heart and respiration rates.

Cullen and Reynoldson (1997) used propofol in five mongrel dogs and observed decrease in arterial pressure and respiratory frequency with transient increase in heart rate. They further observed that propofol in combination with tiltamine zolazepam causes an increase in arterial pressure and heart rate with decrease in respiratory frequency.

Bufalari *et al.* (1998) studied compatibility of propofol with halothane and isoflurane in dogs. They suggested that propofol in combination with these inhalation anaesthetics can be used effectively and safely for dogs in veterinary practice.

Hellebreker *et al.* (1998) studied the effect of combination of medetomidine with propofol or ketamine anasesthesia in dogs. They reported adverse side effects and poor recovery with ketamine as compared to propofol.

Patil *et al.* (1999) studied anaesthetic properties of propofol in dogs. The anaesthetic was administered @ 2.5 mg/kg, 5 mg/kg, 7.5 mg/kg and 10 mg/kg b.wt. without premedication. They observed highly significant difference in heart, pulse, and respiration rates between the groups.

Bettschart *et al*, (2001) used the propofol-medetomidine infusion in ponies to induce long duration of anaesthesia and observed that cardiovascular functions are better with this combination as compared to inhalation anaesthetics. However, in some animals he reported severe hypoxia for which supplementation of oxygen is necessary.

Sharma *et al.* (2001) used propofol in combination with triflupromazine and midazolam preanesthetics in dogs and observed significant increase in heart rate and nonsignificant decrease in rectal temperature and respiratory rate.

Venugopalan *et al.* (2002) recorded significant decrease in rectal temperature, respiratory rate while increase in pulse rate by using propofol - ketamine with or without preanaesthetics in dogs.

Haemato-biochemical studies

Glen and Hunter (1984) recorded peak haemodynamic effects for 2 to 7.5 minutes after administration of propofol.

Lumb and Jones (1984) recorded that repeated doses of thiopentone had a cumulative effect resulting in prolonged periods of anaesthsia. However, Morgan and Legge (1989) observed that propofol had no cumulative effect in dogs, when given repeatedly to maintain anaesthesia. The adverse consequences after accidental perivascular injection were not seen. However, a 5% solution of thiopentone caused severe tissue reaction when injected perivascularly.

Kelawala *et al.* (1991) studied the use of propofol-ketamine in diazepam premedicated goats and reported insignificant decrease in haemoglobin, packed cell volume, total erythrocyte and total leucocyte count. They further observed non significant increase in blood urea nitrogen and serum creatinine but significant increase in blood glucose upto 48 hours.

David (1993) observed non significant changes in the value of haematological and biochemical parameters except an increase in blood glucose level during anaesthesia.

Gill *et al.* (1996) observed increase in haemoglobin concentration and total erythrocyte count and decrease in total leucocyte count after the administration of propofol with acepromazine - meperidine - atropine sulphate as preanaesthetic medication in dogs.

Sharma *et al.* (2001) observed significant increase in neutrophil count, whereas, significant decrease in PCV, lymphocyte, eosinophil and

monocyte count by using propofol in combination with triflupromazine and midazolam in dogs. They further observed non significant decrease in TEC and Hb concentration.

Bayan *et al.* (2002) observed non significant changes in DLC and serum protein while significant increase in blood glucose level after administration of propofol in dogs. They further reported non significant increase in TEC and TLC.

Sharma *et al.* (2002) evaluated the biochemical effect of propofol anaesthesia alone and in combination with triflupromazine and midazolam in dogs. Non significant increase in the values of blood glucose, serum alkaline phosphatase and blood urea nitrogen, whereas non significant decrease in serum protein was observed in all the treatments. Serum glutamic pyruvic transaminase, icterus index and creatinine did not revealed any significant variation in any of the treatments.

Shinkar *et al*, (2002) used propofol with detomidine in dogs and observed excellent anaesthesia and muscle relaxation of longer duration. He further observed that bradycardia and respiratory depressant effects produced by detomidine were minimized by using propofol.

Venugopalan *et al.* (2002) used propofol- ketamine anaesthesia with or without preanaesthetics in dogs and observed significant decrease in TEC, TLC, Hb concentration and PCV.

DIETHYL ETHER

Diethyl ether is an organic compound having two organic radicle attached to an atom of oxygen R-O-R. Paracelsus (1540) invented ether in

medical science and reported its soporific effect on fowl. Furather, it was synthesized by Valerius codus (1540) in Germany. Dr. J.P. Jarksons was the first to use it in animal practice. Diethyl ether is colourless, highly volatile liquid with a pungent odour and irritating vapour. Ether is much inflammable and its vapour with air or oxygen are explosive, hence safety precautions must be undertaken during its use to avoid explosion from sparking of electricity and fire.

Greene (1968) and Lumb and Jones (1984) reported that major portion of ether is exhaled unchanged, while a part is metabolised into ethanol and acetyl aldehyde and subsequently into carbon dioxide in liver. Traces are also eliminated along with feaces urine and other fluids.

Ether induces initial excitement due to irritation of mucous membranes, which is responsible for delirium during induction, followed by reversible generalized central nervous system depression of cortex, medulla and spinal cord in the ascending order (Hall and Clarke, 1983).

Clinical studies

Ether increases the sensitivity of the carotid sinus, aortic arch and baroceptor (Robertson *et al.*, 1956), blocks transmission through sympathetic ganglia (Norman and Lofstron, 1955), which are responsible for fall in arterial blood pressure during the deeper level of anaesthesia after an initial transient rise.

Rex (1973) evaluated the effect of ether and halothane on laryngeal activity in cats and concluded that both stimulate laryngeospasm when administered in high concentration by mask.

Hillidge and Lees (1974) compared the halothane and ether anaesthesia in horses and recorded lesser decrease in cardiac output and greater increase in arterial blood lactate concentration with ether than halothane.

Pandey and Patel (1977) observed increase in pulse rate after administration of ether and correlated it, with stimulation of sympathetic system or due to increased adrenaline secretion.

Duncalf (1982) reported ether as a safest inhalation anaesthetic for clinical anaesthetic management in human beings and animals.

Hall and Clarke (1983) reported that ether produces better relaxation of muscles, as compare to other inhalation anaesthetic agents because of its curare like effect at the neuromuscular junction and depression of transmission through motor fibres. They further reported ether as a safest anaesthetic agent due to its wide safety margin between anaesthetic and toxic doses.

Lumb and Jones (1984) reported induction time of 3 to 10 minutes by using 3.5 to 4.5% concentration of ether as sole inhalation anaesthetic agent and further recorded increased cardiac output during induction with ether inhalation followed by decrease in deep surgical anaesthesia.

Vickers *et al.* (1984) reported that diethyl ether induces initial respiratory stimulation followed by depression in deepest plane of surgical anaesthesia.

Haemato – biochemical studies

Pandey and Patel (1977) and Lumb and Jones (1984) described that ether inhalation induces haemoconcentration with an increase in the red blood cells and haemoglobin concentration accompained by decrease in plasma volume. They also reported leucocytosis after ether inhalation.

Hall and Clarke (1983) reported that ether irritates the kidney tissue and thereby depresses the kidney function as well as urine out put transiently.

Vickers *et al.* (1984) observed hyperglycaemia, decreased serum bicarbonate (acidosis), serum potassium and rise in lactate : pyruvate ratio after administration of ether as inhalation anaesthetic.

Clarke *et al.* (1993) recorded depressed liver function and secretion of bile during the anaesthesia by reducing liver blood flow and oxygen delivery.

~~~ Materials and Methods

MATERIALS AND METHODS

Six apparently healthy mongrel adult dogs of either sex weighing approximately 10-20 kg were used for the present experiment. The dogs were kept on a uniform diet and management during the entire period of experiment. All the dogs were dewormed with praziquintol and albendazol[1] and vaccinated against rabies 10 days prior to commencement of actual experiment. These animals were kept under pre experimental observation for 10 days. Thorough clinical examination, haematological and biochemical estimations were conducted with a view to obtain baseline values before commencement of actual experiment.

The clinical parameters namely rectal temperature, pulse and respiration rates were recorded in all the animals. Three blood samples were collected from each animal and analyzed for the hematological attributes i.e. total erythrocyte count (TEC), total leucocytes count (TLC), differential leucocytes count (DLC), haemoglobin concentration (Hb) and packed cell volume (PCV). The biochemical parameters analyzed were plasma glucose, total protein, alanine amino transferase (ALT), alkaline phosphatase (AP), urea nitrogen and creatinine.

PLAN OF EXPERIMENT

The total duration of study was approximately 3 months starting from January to March 2003. Each dog was subjected to 3 different treatments and each of which lasted for four days. A rest period of eight days was provided before the start of next treatment. Each experimental animals was starved for 24 hours prior to treatment. Only one animal was used for the specific treatment in a day.

[1] Praziquantal 25mg, Albendazole 300mg : Praziplus, petcare.

Residual effect of the preceding treatment was ascertained by restoration of normal values of different haematological and biochemical profiles. The plan of experiment was as follows: -

ANIMAL No.	TREATMENTS		
1.	T I	T II	T III
2.	T II	T III	T I
3.	TIII	T I	T II
4.	T I	T II	T III
5.	T II	T III	T I
6.	TIII	T I	T II

METHODOLOGY

Three treatments given to each of all the six dogs were as follows:-

TREATMENT I :- ATROPINE SULPHATE[2] + TRIFLUPROMAZINE HYDROCHLORIDE[3] + PROPOFOL[4] + ETHER[5]

Atropine sulphate @ 0.05 mg/kg b.wt. I.M., before triflupromazine hydrochloride @ 1mg/kg b. wt. I.V. followed by propofol (1%) I.V., 10 minutes after the administration of triflupromazine, till the loss of paedal reflex.The anaesthesia was maintained for half an hour with anaesthetic ether using semiclose method.

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[2] Atropine sulphate - Haryana Biological India P. Ltd., Gurgoan.

[3] Triflupromazine hydrochloride - Siquil, Sarabhai Chemicals, Baroda.

[4] Propofol - Profol (1 %), Claris Lifesciences Ltd., Ahmedabad.

[5] Anaesthetic ether- TKM Pharma, Hyderabad 500020.

TREATMENT II :- ATROPINE SULPHATE + DIAZEPAM[6] + PROPOFOL + ETHER

Atropine sulphate @ 0.05 mg/kg b. wt. I.M., followed by diazepam @ 2 mg / kg b. wt. I.V. Propofol and anaesthetic ether were administered as in treatment I, ten minutes after the administration of diazepam.

TREATMENT III :- ATROPINE SULPHATE + XYLAZINE[7]+ PROPOFOL + ETHER

Atropine sulphate @ 0.05mg/kg b.wt. I.M. was followed by xylazine @ 1.5 mg/kg b.wt. I.M. The propofol and anaesthetic ether were administered as in treatment I, ten minutes after the administration of xylazine.

PARAMETERS OF STUDY

A. CLINICAL

The rectal temperature, heart and respiration rates (per minute) were recorded at 0, 10, 20, 30 minutes and at 1, 2, 3, 4, 5, 6, 9, 24 and 48 hours post treatment. The '0' hour values were recorded just before the start of treatment and were treated as control.

The duration of surgical anaesthesia was the time interval between loss of paedal reflex and its reappearance. The complete recovery from anaesthesia was the time interval between reappearance of paedal reflex to return of all reflexes with unassisted standing by the animal.

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[6] Diazepam :- Calmpose, Ranbaxy Laboratories Ltd., Mumbai.

[7] Xylazine :- Rompun (2%) Bayer (India) Ltd., Banglore.

B. HAEMATOLOGICAL

The blood samples were collected from the cephalic or saphenous vein at 0 hour i.e. just before the start of treatment (control value) and subsequently at 1,3,6,9,24, 48 and 72 hours post treatment using heparin sodium[8] as anticoagulant. Each sample was analyzed for the estimation of following haematological attributes using standard procedures described by Jain (1986).

(i) Total Erythrocyte and Leucocyte Counts

Total erythrocyte (million /cu. mm.) and leucocyte counts (thousand /cu.mm.) were carried out by using bright line Neubeaur haemocytometer.

Gower's and Turk's diluting fluids were used for the estimation of TEC and TLC respectively.

(ii) Differential Leucocyte Count

The differential leucocyte count was carried out with freshly prepared thin blood smear after staining with Leishman's stain. The proportion of different leucocytes was expressed in percentage.

(iii) Packed Cell Volume

The packed cell volume (%) was determined by using the Wintrobe's haematocrit tube centrifuged at 3000 rpm for 30 minutes.

(iv) Haemoglobin Concentration

The haemoglobin concentration (gm per cent) in blood was determined by the acid haematin method using Sahli's haemoglobinometer.

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[8] Heparin sodium – Beparine, Biological E. Limited, Patancheru.

C. BIOCHEMICAL

The biochemical parameters in the blood samples were estimated at the same intervals as for the haematological studies. A part of the collected blood was centrifuged at 5000 rpm for 10 minutes immediately after collection, for separating the plasma. The collected plasma was used for the estimation of following biochemical parameters viz.

1. Plasma glucose (Trinder, 1969).
2. Plasma total protein (Vatzidis,1977).
3. Plasma alkaline phosphatase (Bretendiere, 1977).
4. Plasma alanine amino transferase or plasma glutamic pyruvic transminase (Bergmmeyer, 1980).
5. Plasma urea nitrogen (Hallett, 1971).
6. Plasma creatinine (Kammcraat, 1978).

All the above parameters were estimated by using semiauto analyzer "State fax 2000" using "Ranbaxy" diagnostic kits. The values of plasma glucose, creatinine, urea nitrogen were expressed in mg/dl, while plasma protein in gm/dl and plasma alkaline phosphatase and alanine amino transferase in IU/L.

Statistical Analysis of the Data

Statistical analysis was done using analysis of variance for heirarchical design with treatment as main heirarchy and intervals within treatment as sub heirarchy. The standard procedure was used as outlined by Snedecor and Corchran (1968).

~~~ Results

RESULTS

In the present study clinical, haematological and biochemical changes were recorded after the administration of propofol and anaesthetic ether in combination with triflupromazine hydrochloride, diazepam or xylazine as preanaesthetics in dogs.

(A) CLINICAL STUDIES

The clinical parameters recorded in response to various treatments for duration and complete recovery from anaesthesia along with doses of propofol and ether are presented in table 1.

Duration of anaesthesia

Duration of surgical anaesthesia in the present study was the time interval between the loss of paedal reflex after I.V. administration of propofol and its reappearance. It was 38.33 ± 4.40, 34.16 ± 1.35 and 46.83 ± 5.32 minutes in treatments I, II and III respectively.

Complete recovery

Complete recovery from anaesthesia was the time interval between reappearance of paedal reflex to return of all reflexes with unassisted standing. The time required for the complete recovery from anaesthesia was 60.83 ± 18.40 minutes in treatment I, 68.33 ± 22.45 minutes in treatment II and 43.33 ± 9.54 minutes in treatment III.

AFTER ADMINISTRATION OF TRIFLUPROMAZINE AND PROPOFOL.

ADMINISTRATION OF ANAESTHETIC ETHER BY SEMICLOSE METHOD

COMPLETE RECOVERY AFTER TRIFLUPROMAZINE, PROPOFOL AND ANAESTHETIC ETHER.

TEN MINUTES AFTER THE ADMINISTRATION OF DIAZEPAM.

AFTER ADMINISTRATION OF DIAZEPAM AND PROPOFOL.

COMPLETE RECOVERY AFTER DIAZEPAM, PROPOFOL AND ANAESTHETIC ETHER.

TEN MINUTES AFTER ADMINISTRATION OF XYLAZINE.

AFTER ADMINISTRATION OF XYLAZINE AND PROPOFOL.

COMPLETE RECOVERY AFTER ADMINISTRATION OF XYLAZINE, PROPOFOL AND ANAESTHETIC ETHER.

Table 1: Clinical observations among different treatments in dogs.

	Treatment – I	Treatment – II	Treatment – III
Duration of anaesthesia (minutes)	38.33 ± 4.40	34.16 ± 1.35	46.83 ± 5.32
Complete recovery from anaesthesia after cesation of ether (minutes)	60.83 ± 18.40	68.33 ± 22.45	43.33 ± 9.54
Dose of propofol (mg/kg)	4.28 ± 0.47	4.41 ± 0.40	2.82 ± 0.62
Dose of ether (ml/kg)	3.53 ± 0.95	3.54 ± 0.60	3.60 ± 0.42

Treatments :

I Atropine sulphate @ 0.05 mg/kg I.M. + triflupromazine hydrochloride @ 1mg/kg I.V. + propofol I.V. + anaesthetic ether.

II Atropine sulphate @ 0.05 mg/kg I.M. + diazepam @ 2 mg/kg I.V. + propofol I.V. + anaesthetic ether.

III Atropine sulphate @ 0.05 mg/kg I.M. + xylazine @ 1.5 mg/kg I.M. + propofol I.V. + anaesthetic ether.

Table 2: Mean values (±SE) of Temperature (^{0}F) at different time intervals following three treatments in dogs.

Time (Minutes/Hours)	Treatment – I	Treatment – II	Treatment – III
0	101.8 ± 0.13	101.7 ± 0.31	101.8 ± 0.23
10	100.7 ± 0.52	100.8 ± 0.44	101.4 ± 0.43
20	100.3 ± 0.58	100.4 ± 0.47	101.3 ± 0.56
30	100.5 ± 0.57	100.3 ± 0.56	101.3 ± 0.75
1	100.3 ± 0.51	100.2 ± 0.70	100.9 ± 0.75
2	100.5 ± 0.32	101.2 ± 0.45	100.8 ± 0.71
3	100.7 ± 0.23	101.2 ± 0.18	101.0 ± 0.62
4	100.4 ± 0.26	101.2 ± 0.34	101.3 ± 0.62
5	100.6 ± 0.27	101.0 ± 0.35	101.4 ± 0.30
6	100.8 ± 0.35	101.2 ± 0.29	101.8 ± 0.28
9	100.8 ± 0.22	101.3 ± 0.29	101.6 ± 0.14
24	102.1 ± 0.19	101.5 ± 0.24	101.6 ± 0.20
48	102.2 ± 0.21	101.7 ± 0.28	101.9 ± 0.33

Treatments :

I Atropine sulphate @ 0.05 mg/kg I.M. + triflupromazine hydrochloride @ 1mg/kg I.V. + propofol I.V. + anaesthetic ether.

II Atropine sulphate @ 0.05 mg/kg I.M. + diazepam @ 2 mg/kg I.V. + propofol I.V. + anaesthetic ether.

III Atropine sulphate @ 0.05 mg/kg I.M. + xylazine @ 1.5 mg/kg I.M. + propofol I.V. + anaesthetic ether.

Table 3 : Mean values (±SE) of Respiration Rate (per minutes) at different time intervals following three treatments in dogs.

Time (Minutes/Hours)	Treatment – I	Treatment – II	Treatment – III
0	22.5 ± 2.40	25.1 ± 3.20	24.3 ± 1.60
10	26.3 ± 3.89	26.8 ± 3.00	19.1 ± 1.91
20	31.6 ± 7.27*	27.0 ± 2.71	18.0 ± 1.26
30	42.8 ± 8.94*	41.1 ± 5.67*	16.8 ± 0.79
1	28.5 ± 5.37	26.8 ± 4.20	13.5 ± 1.71*
2	18.0 ± 1.43	26.1 ± 2.38	13.5 ± 1.90*
3	16.3 ± 2.48	24.8 ± 1.51	15.3 ± 1.35*
4	16.8 ± 2.15	23.1 ± 2.10	16.3 ± 0.55
5	16.8 ± 2.46	22.8 ±1.80	17.3 ± 1.02
6	17.1 ± 2.27	21.3 ± 1.22	17.5 ± 0.95
9	18.5 ± 2.04	20.0 ± 1.50	18.0 ± 1.29
24	20.1 ± 2.28	21.8 ±1.10	22.1 ± 1.30
48	20.6 ± 2.23	22.0 ±0.77	22.1 ± 1.01

Least Significant Difference (L.S.D.) = 8.28 at P = 0.05

Treatments :

I Atropine sulphate @ 0.05 mg/kg I.M. + trifluprom azine hydrochloride @ 1mg/kg I.V. + propofol I.V. + anaesthetic ether.

II Atropine sulphate @ 0.05 mg/kg I.M. + diazepam @ 2 mg/kg I.V. + propofol I.V. + anaesthetic ether.

III Atropine sulphate @ 0.05 mg/kg I.M. + xylazine @ 1.5 mg/kg I.M. + propofol I.V. + anaesthetic ether.

* Significant at 5% level as compared to 0 hour value.

Dose of propofol

The dose of propofol used to produce surgical anaesthesia was 4.28 ± 0.47 mg/kg b.wt. in treatment I, 4.41 ± 0.40 mg/kg b.wt. in treatment II and 2.82 ± 0.62 mg/kg b.wt. in treatment III.

Dose of ether

Five minutes after the induction of general anaesthesia with propofol intravenously the anaesthesia was maintained for half an hour with anaesthetic ether using semiclosed method. The amount of anaesthetic ether used was 3.53 ± 0.95, 3.54 ± 0.60 and 3.60 ± 0.42 ml/kg b. wt. in treatments I, II and III respectively.

Rectal temperature

The mean values of rectal temperature (^{0}F) are presented in table 2.

A non significant decrease in rectal temperature was observed in all the three treatments. The minimum values of 100.3 ± 0.51, 100.2 ± 0.70 and 100.8 ± 0.71 °F from control values of 101.8 ± 0.13, 101.7 ± 0.31 and 101.8 ± 0.23 °F were observed at 1 hour in treatments I, II and at 2 hours in treatment III respectively. There after the values fluctuated between 100.4 ± 0.26 to 102.2 ± 0.21, 101.0 ± 0.35 to 101.7 ± 0.28 and 101.0 ± 0.62 to 101.9 ± 0.33 ^{0}F in treatments I, II and III respectively.

Respiration rate

The mean values of respiration rate (per minute) are showed in table 3.

Table 4 : Mean values (±SE) of Heart Rate (per minute) at different time intervals following three treatments in dogs.

Time (Minutes/Hours)	Treatment – I	Treatment – II	Treatment – III
0	103.3 ± 2.47	108.6 ± 2.80	100.8 ± 5.68
10	156.5 ± 5.97*	149.1 ± 9.39*	142.3 ± 9.24*
20	162.0 ± 5.18*	152.0 ± 7.83*	150.5 ± 3.08*
30	160.0 ± 6.19*	167.3 ± 3.52*	150.6 ± 5.90*
1	145.5 ± 3.93*	145.6 ± 6.00*	112.6 ± 10.00
2	125.1± 8.48	134.5 ± 6.97	92.5 ± 6.34
3	120.5 ± 5.34	128.5 ± 6.99	87.8 ± 8.08
4	106.6 ± 5.42	107.6 ± 8.69	86.3 ± 6.86
5	97.1 ± 3.24	102.0 ± 5.41	86.1 ± 4.71
6	98.3 ± 6.91	100.8 ± 4.50	90.1 ± 6.03
9	98.3 ± 4.77	100.0 ± 4.28	96.3 ± 6.45
24	103.1 ± 1.07	105.8 ± 3.00	100.8 ± 5.23
48	103.0 ± 1.82	105.0 ± 2.58	101.1 ± 5.62

Treatments :

I Atropine sulphate @ 0.05 mg/kg I.M. + triflupromazine hydrochloride @ 1mg/kg I.V. + propofol I.V. + anaesthetic ether.

II Atropine sulphate @ 0.05 mg/kg I.M. + diazepam @ 2 mg/kg I.V. + propofol I.V. + anaesthetic ether.

III Atropine sulphate @ 0.05 mg/kg I.M. + xylazine @ 1.5 mg/kg I.M. + propofol I.V. + anaesthetic ether.

* Significant at 5% level as compared to 0 hour value.

Table 5: Mean values (±SE) of Total Erythrocyte Count (million/cu.mm.) at different time intervals following three treatments in dogs.

Time (Hours)	Treatment – I	Treatment – II	Treatment – III
0	6.2 ± 0.20	5.8 ± 0.29	6.8 ± 0.20
1	5.4 ± 0.15	5.6 ± 1.22	5.8 ± 0.46
3	5.4 ± 0.18	5.4 ± 1.22	5.6 ± 0.30
6	5.6 ± 0.17	5.9 ± 0.26	5.7 ± 0.28
9	4.3 ± 0.31	5.6 ± 0.29	6.2 ± 0.60
24	6.0 ± 0.42	5.8 ± 0.30	5.4 ± 0.20
48	6.3 ± 0.42	6.1 ± 0.33	5.9 ± 0.21
72	6.1 ± 0.16	5.4 ± 0.37	6.4 ± 0.30

Treatments :

I Atropine sulphate @ 0.05 mg/kg I.M. + trifluprom azine hydrochloride @ 1mg/kg I.V. + propofol I.V. + anaesthetic ether.

II Atropine sulphate @ 0.05 mg/kg I.M. + diazepam @ 2 mg/kg I.V. + propofol I.V. + anaesthetic ether.

III Atropine sulphate @ 0.05 mg/kg I.M. + xylazine @ 1.5 mg/kg I.M. + propofol I.V. + anaesthetic ether.

Respiration rate increased significantly ($P<0.05$) from 0 hour values of 22.5 ± 2.40 and 25.1 ± 3.20 per minute to maximum values of 42.8 ± 8.94 and 41.1 ± 5.67 per minute at 30 minutes in treatments I and II respectively. Thereafter, non significant decrease was observed and the values returned to the normal level at 48 hours post treatment. In treatment III significant decrease ($P<0.05$) was observed from 1 to 3 hours with minimum value of 13.5 ± 1.71 at 1 hour from control value of 24.3 ± 1.60 per minute. There after non significant increase was observed and values returned to normal at 48 hours.

Heart rate

The mean values of heart rate (per minute) are depicted in table 4.

A significant increase ($P<0.05$) in heart rate was observed from 10 minutes to 1 hour and the maximum values of 162.0 ± 5.18 and 167.3 ± 3.52 from the control values of 103.3 ± 2.47 and 108.6 ± 2.80 per minute were recorded at 20 and 30 minutes in treatments I and II respectively. While in treatment III significant increase ($P<0.05$) was observed from 10 to 30 minutes with the maximum value of 150.6 ± 5.90 from the control value of 100.8 ± 5.68 per minute at 30 minutes. The values of heart rate thereafter decreased gradually in all the three treatments and reached near to preadministration values within 48 hours.

(B) HAEMATOLOGICAL STUDIES

Total erythrocyte count

The mean values of total erythrocyte count (million/cu.mm.) are presented in table 5.

Table 6 : Mean values (±SE) of Total Leucocyte Count (thousand/cu.mm.) at different time intervals following three treatments in dogs.

Time (Hours)	Treatment – I	Treatment – II	Treatment – III
0	11.1 ± 1.58	10.9 ± 0.92	11.5 ± 1.24
1	7.7 ± 1.02	11.2 ±1.40	11.4 ± 1.43
3	8.6 ± 0.98	13.3 ± 1.77	12.9 ± 1.77
6	10.8 ± 1.49	11.3 ± 0.45	14.8 ± 2.06
9	10.0 ± 1.64	11.9 ± 1.08	11.4 ± 0.61
24	9.8 ± 1.22	10.4 ± 1.16	11.5 ± 1.01
48	10.2 ± 0.99	11.1 ± 1.46	11.9 ± 0.76
72	10.6 ± 0.62	11.8 ± 1.51	10.7 ± 1.29

Treatments :

I Atropine sulphate @ 0.05 mg/kg I.M. + triflupromazine hydrochloride @ 1 mg/kg I.V. + propofol I.V. + anaesthetic ether.

II Atropine sulphate @ 0.05 mg/kg I.M. + diazepam @ 2 mg/kg I.V. + propofol I.V. + anaesthetic ether.

III Atropine sulphate @ 0.05 mg/kg I.M. + xylazine @ 1.5 mg/kg I.M. + propofol I.V. + anaesthetic ether.

Table 7 : Mean values (±SE) of Packed Cell Volume (per cent) at different time intervals following three treatments in dogs.

Time (Hours)	Treatment – I	Treatment – II	Treatment – III
0	46.0 ± 1.73	49.1 ± 2.05	44.0 ± 2.16
1	40.3 ± 0.41	47.8 ± 1.86	42.5 ± 3.44
3	36.8 ± 1.92	43.3 ± 2.20	41.0 ± 1.66
6	37.1 ± 1.70	40.1 ± 5.39	42.6 ± 1.40
9	38.3 ± 2.61	40.3 ± 2.38	43.1 ± 1.40
24	45.0 ± 2.52	42.3 ± 3.13	43.5 ± 2.29
48	43.6 ± 1.99	42.8 ± 2.60	44.1 ± 4.19
72	44.4 ± 1.83	45.6 ± 2.17	41.3 ± 2.27

Treatments :

I Atropine sulphate @ 0.05 mg/kg I.M. + triflupromazine hydrochloride @ 1mg/kg I.V. + propofol I.V. + anaesthetic ether.

II Atropine sulphate @ 0.05 mg/kg I.M. + diazepam @ 2 mg/kg I.V. + propofol I.V. + anaesthetic ether.

III Atropine sulphate @ 0.05 mg/kg I.M. + xylazine @ 1.5 mg/kg I.M. + propofol I.V. + anaesthetic ether.

A non significant decreasing trend was observed in all the three treatments. The minimum values of 5.4 ± 0.15, 5.4 ± 1.22 and 5.6 ± 0.30 from control values of 6.2 ± 0.20, 5.8 ± 0.29 and 6.8 ± 0.20 million /cu. mm. were observed at 1 hour in treatment I and at 3 hours in treatments II and III respectively. Thereafter, the values fluctuated between 4.3 ± 0.31 to 6.3 ± 0.42, 5.4 ± 0.37 to 6.1 ± 0.33 and 5.4 ± 0.20 to 6.4 ± 0.30 million /cu. mm. in treatments I, II and III respectively.

Total leucocyte count

The mean values of total leucocyte count (thousand / cu.mm.) at various intervals with different treatments are shown in table 6.

A non significant change in total leucocyte count was observed in all the three treatments. The values fluctuated between 7.7 ±1.02 to 11.1 ±1.58 thousand / cu.mm. in treatment I, 10.4±1.16 to 13.3±1.77 thousand/cu. mm. in treatment II and 10.7 ± 1.29 to 14.8 ± 2.06 thousand /cu. mm. in treatment III.

Packed cell volume

The mean values of packed cell volume (per cent) are depicted in table 7.

The packed cell volume showed non significant decreasing trend in all the three treatments. The control values of 46.0 ± 1.73, 49.1 ± 2.05 and 44.0 ± 2.16 per cent decreased to minimum values of 36.8 ± 1.92, 40.1 ± 5.39 and 41.0 ± 1.66 per cent at 3 hours in treatments I and III and at 6 hours in treatment II respectively. Thereafter, gradual increase was observed and the normal values were attained at 72 hours post treatments.

Table 8 : Mean values (±SE) of Haemoglobin Concentration (gm per cent) at different time intervals following three treatments in dogs.

Time (Hours)	Treatment – I	Treatment – II	Treatment – III
0	13.2 ± 0.47	12.8 ± 0.54	12.9 ± 0.43
1	11.7 ± 0.42	12.6 ± 0.43	11.8 ± 0.33
3	10.7 ± 0.31	12.5 ± 0.53	12.5 ± 0.55
6	11.2 ± 0.46	11.9 ± 0.57	12.6 ± 0.41
9	10.3 ± 0.61	12.1 ± 0.84	12.6 ± 0.47
24	11.6 ± 0.66	12.8 ± 0.78	12.7 ± 0.47
48	12.6 ± 0.73	12.3 ± 0.80	12.9 ± 0.42
72	12.9 ± 0.45	12.3 ± 0.51	12.7 ± 0.45

Treatments :

I Atropine sulphate @ 0.05 mg/kg I.M. + triflupromazine hydrochloride @ 1mg/kg I.V. + propofol I.V. + anaesthetic ether.

II Atropine sulphate @ 0.05 mg/kg I.M. + diazepam @ 2 mg/kg I.V. + propofol I.V. + anaesthetic ether.

III Atropine sulphate @ 0.05 mg/kg I.M. + xylazine @ 1.5 mg/kg I.M. + propofol I.V. + anaesthetic ether.

Table 9 : Mean values (±SE) of Neutrophil Count (per cent) at different time intervals following three treatments in dogs.

Time (Hours)	Treatment – I	Treatment – II	Treatment – III
0	56.0 ± 2.86	56.3 ± 1.88	58.3 ± 3.12
1	67.5 ± 0.88*	67.8 ± 4.97*	74.6 ± 3.98*
3	68.5 ± 1.47*	74.1 ± 1.72*	71.6 ± 3.61*
6	73.3 ± 2.15*	76.5 ± 2.14*	69.5 ± 2.90*
9	67.0 ±2.43*	68.0 ± 1.71*	66.5 ± 2.29*
24	62.0± 1.91	64.5 ± 4.51	64.1 ± 2.35
48	60.0 ± 1.94	58.0 ± 2.38	59.3 ± 2.72
72	57.0 ± 1.03	55.1 ± 2.35	57.0 ± 2.30

Least Significant Difference (L.S.D.) = 7.81 at P = 0.05

Treatments :

I Atropine sulphate @ 0.05 mg/kg I.M. + triflupromazine hydrochloride @ 1 mg/kg I.V. + propofol I.V. + anaesthetic ether.

II Atropine sulphate @ 0.05 mg/kg I.M. + diazepam @ 2 mg/kg I.V. + propofol I.V. + anaesthetic ether.

III Atropine sulphate @ 0.05 mg/kg I.M. + xylazine @ 1.5 mg/kg I.M. + propofol I.V. + anaesthetic ether.

* Significant at 5% level as compared to 0 hour value.

Table 10 : Mean values (±SE) of Eosinophil Count (per cent) at different time intervals following three treatments in dogs.

Time (Hours)	Treatment – I	Treatment – II	Treatment – III
0	3.1 ± 0.79	5.5 ± 0.42	3.8 ± 0.60
1	7.0 ± 0.81	5.3 ± 1.14	3.1 ± 0.70
3	6.1 ± 1.19	4.3 ± 0.91	5.1 ± 0.94
6	4.1 ± 0.95	4.3 ± 0.71	5.5 ± 0.76
9	2.6 ± 0.33	4.1 ± 0.54	5.5 ± 1.17
24	3.1 ± 0.47	4.0 ± 0.73	4.0 ± 1.00
48	2.6 ± 0.80	5.0 ± 0.42	3.8 ± 0.47
72	4.8 ± 0.70	4.1 ± 0.47	4.3 ± 0.33

Treatments :

I Atropine sulphate @ 0.05 mg/kg I.M. + trifluopromazine hydrochloride @ 1 mg/kg I.V. + propofol I.V. + anaesthetic ether.

II Atropine sulphate @ 0.05 mg/kg I.M. + diazepam @ 2 mg/kg I.V. + propofol I.V. + anaesthetic ether.

III Atropine sulphate @ 0.05 mg/kg I.M. + xylazine @ 1.5 mg/kg I.M. + propofol I.V. + anaesthetic ether.

Haemoglobin concentration

The mean value of haemoglobin concentration (gm per cent) are shown in table 8.

A non significant gradual decrease in haemoglobin concentration was observed in all the three treatments. The control values of 13.2 ±0.47, 12.8 ± 0.54 and 12.9 ± 0.43 gm per cent decreased to minimum values of 10.3 ± 0.61, 11.9 ± 0.57 and 11.8 ± 0.33 gm per cent at 9, 6 and 1 hour in treatments I, II and III respectively. This was followed by gradual increase and from 48 hour onward the values returned near to normal.

Differential leucocyte count (DLC)

The mean values of different leucocyte count (per cent) are shown in table 9 to 12.

(i) Neutrophil Count

A significant increase ($P<0.05$) in neutrophil count was recorded from 1 to 9 hours with the maximum value of 73.3 ± 2.15 at 6 hours from its control value of 56.0 ± 2.86 per cent in treatment I. In treatment II it was significantly ($P<0.05$) high from 1 to 9 hours with the maximum value of 76.5 ± 2.14 at 6 hours from the control value of 56.3 ± 1.88 per cent. However in treatment III the control value of 58.3 ±3.12 increased to maximum value of 74.6 ±3.98 per cent at 1 hour. In all the three treatments the values recorded at 72 hours were near to normal (Table 9).

(ii) Eosinophil count

The eosinophil count (Table 10) showed non significant difference in all the three treatments and the values fluctuated between 2.6 ± 0.33 to

Table 11 : Mean values (±SE) of Monocyte Count (per cent) at different time intervals following three treatments in dogs.

Time (Hours)	Treatment – I	Treatment – II	Treatment – III
0	3.5 ± 0.67	3.3 ± 0.42	3.0 ± 0.57
1	5.8 ± 0.98*	2.3 ± 0.33	2.6 ± 0.55
3	7.1 ± 0.65*	3.0 ± 0.85	4.8 ± 0.47*
6	5.1 ± 0.80*	4.0 ± 0.57*	4.8 ± 0.30*
9	5.3 ± 0.33*	3.5 ± 0.34	4.3 ± 0.30*
24	4.3 ± 0.42	3.8 ± 0.74	2.5 ± 0.56
48	3.6 ± 0.55	2.8 ± 0.54	2.1 ± 0.40
72	2.6 ± 0.33	3.1 ± 0.40	1.8 ± 0.30

Least Significant Difference (L.S.D.) = 1.55 at P = 0.05

Treatments :

I Atropine sulphate @ 0.05 mg/kg I.M. + triflupromazine hydrochloride @ 1 mg/kg I.V. + propofol I.V. + anaesthetic ether.

II Atropine sulphate @ 0.05 mg/kg I.M. + diazepam @ 2 mg/kg I.V. + propofol I.V. + anaesthetic ether.

III Atropine sulphate @ 0.05 mg/kg I.M. + xylazine @ 1.5 mg/kg I.M. + propofol I.V. + anaesthetic ether.

* Significant at 5% level as compared to 0 hour value.

Table 12 : Mean values (±SE) of Lymphocyte Count (per cent) at different time intervals following three treatments in dogs.

Time (Hours)	Treatment – I	Treatment – II	Treatment – III
0	39.3 ± 2.31	35.0 ± 1.86	34.8 ± 3.07
1	19.5 ± 2.01*	22.6 ± 4.03*	19.6 ± 4.08*
3	17.3 ± 1.90*	18.5 ± 1.54*	19.0 ± 4.02*
6	16.8 ± 2.60*	15.1 ± 2.50*	20.1 ± 3.07*
9	24.8 ± 2.24*	24.3 ± 1.94*	23.5 ± 2.52*
24	30.5 ± 2.10*	28.0 ± 4.31	29.3 ± 2.94
48	33.6 ± 2.55	34.1 ± 2.24	34.6 ± 2.94
72	35.5 ± 1.52	37.5 ± 2.56	36.8 ± 2.42

Least Significant Difference (L.S.D.) = 8.38 at P = 0.05

Treatments :

I Atropine sulphate @ 0.05 mg/kg I.M. + triflupromazine hydrochloride @ 1mg/kg I.V. + propofol I.V. + anaesthetic ether.

II Atropine sulphate @ 0.05 mg/kg I.M. + diazepam @ 2 mg/kg I.V. + propofol I.V. + anaesthetic ether.

III Atropine sulphate @ 0.05 mg/kg I.M. + xylazine @ 1.5 mg/kg I.M. + propofol I.V. + anaesthetic ether.

* Significant at 5% level as compared to 0 hour value.

Table 13 : Mean values (±SE) of Plasma Glucose (mg/dl) at different time intervals following three treatments in dogs.

Time (Hours)	Treatment – I	Treatment – II	Treatment – III
0	85.6 ± 5.89	75.4 ± 6.90	79.0 ± 11.14
1	120.5 ± 12.70*	124.7 ± 12.77*	158.4 ± 27.77*
3	105.1 ± 4.77*	111.8 ± 11.20*	91.7 ± 7.68
6	95.1 ± 4.90	102.0 ± 6.49*	90.4 ± 7.12
9	93.0 ± 7.06	96.6 ± 7.75	87.6 ± 6.42
24	92.6 ± 5.2	83.9 ± 4.09	80.6 ± 4.31
48	89.2 ± 5.62	85.8 ± 5.25	83.9 ± 3.29
72	95.9 ±3.73	81.2 ± 4.60	86.8 ± 7.14

Least Significant Difference (L.S.D.) = 25.83 at P = 0.05

Treatments :

I Atropine sulphate @ 0.05 mg/kg I.M. + triflupromazine hydrochloride @ 1mg/kg I.V. + propofol I.V. + anaesthetic ether.

II Atropine sulphate @ 0.05 mg/kg I.M. + diazepam @ 2 mg/kg I.V. + propofol I.V. + anaesthetic ether.

III Atropine sulphate @ 0.05 mg/kg I.M. + xylazine @ 1.5 mg/kg I.M. + propofol I.V. + anaesthetic ether.

* Significant at 5% level as compared to 0 hour value.

7.0 ± 0.81, 4.0 ± 0.73 to 5.5 ± 0.42 and 3.1 ± 0.70 to 5.5 ± 0.76 per cent in treatments I, II and III respectively.

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(iii) Monocyte count

The monocyte count increased significantly ($P<0.05$) in all the three treatments. The maximum values of monocyte count 7.1 ± 0.65, 4.0 ± 0.57 and 4.8 ± 0.30 from control values of 3.5 ± 0.67, 3.3 ± 0.42 and 3.0 ± 0.57 were observed at 3 hours in treatment I, at 6 hours in treatments II and III respectively (Table 11).

(iv) Lymphocyte count

Significant decrease ($P<0.05$) in the values of lymphocyte (Table 12) count was observed from 1 to 9 hours in all the three treatments. The control values of 39.3 ± 2.31, 35.0 ± 1.86 and 34.8 ± 3.07 decreased to minimum values of 16.8 ± 2.60, 15.1 ± 2.50 and 19.0 ± 4.02 per cent at 6 hours in treatments I and II, while at 3 hours in treatment III respectively. Thereafter, the values increased gradually and returned near to control values at 72 hours post treatment.

(v) Basophil Count

Basophils were seen occasionally in all the three treatments.

(C) BIOCHEMICAL STUDIES

Plasma glucose

Change in plasma glucose level after different treatments (mg/dl) are presented in table 13.

Table 14 : Mean values (±SE) of Plasma Protein (gm/dl) at different time intervals following three treatments in dogs.

Time (Hours)	Treatment – I	Treatment – II	Treatment – III
0	6.6 ± 0.21	6.2 ± 0.36	6.0 ± 0.32
1	6.1 ± 0.22	6.4 ± 0.29	5.7 ± 0.15
3	6.1 ± 0.20	6.2 ± 0.32	5.7 ± 0.18
6	5.9 ± 0.24	6.0 ± 0.25	6.6 ± 0.32
9	6.1 ± 0.40	6.2 ± 0.23	6.5 ± 0.40
24	6.5 ± 0.24	6.2 ± 0.23	6.2 ± 0.34
48	5.8 ± 0.27	5.8 ± 0.37	5.9 ± 0.17
72	6.1 ± 0.48	6.0 ± 0.22	6.1 ± 0.29

Treatments :

I Atropine sulphate @ 0.05 mg/kg I.M. + triflupromazine hydrochloride @ 1mg/kg I.V. + propofol I.V. + anaesthetic ether.

II Atropine sulphate @ 0.05 mg/kg I.M. + diazepam @ 2 mg/kg I.V. + propofol I.V. + anaesthetic ether.

III Atropine sulphate @ 0.05 mg/kg I.M. + xylazine @ 1.5 mg/kg I.M. + propofol I.V. + anaesthetic ether.

Table 15 : Mean values (±SE) of Plasma Alanine Aminotransferase (IU/L) at different time intervals following three treatments in dogs.

Time (Hours)	Treatment – I	Treatment – II	Treatment – III
0	19.7 ± 2.96	27.8 ±5.21	18.9 ± 2.51
1	22.8 ± 4.75	33.2 ± 5.14	21.0 ± 3.14
3	21.1 ± 6.65	34.7 ± 6.39	22.2 ± 3.16
6	20.3 ± 5.50	28.3 ± 5.51	20.2 ± 2.62
9	22.0 ± 5.02	32.2 ± 6.97	25.0 ± 4.10
24	23.5 ± 4.74	30.0 ± 4.50	22.3 ± 3.39
48	23.5 ± 4.56	22.5 ± 3.46	22.4 ± 4.56
72	21.6 ± 3.41	21.7 ± 2.85	21.7 ± 3.30

Treatments :

I Atropine sulphate @ 0.05 mg/kg I.M. + trifluprom azine hydrochloride @ 1mg/kg I.V. + propofol I.V. + anaesthetic ether.

II Atropine sulphate @ 0.05 mg/kg I.M. + diazepam @ 2 mg/kg I.V. + propofol I.V. + anaesthetic ether.

III Atropine sulphate @ 0.05 mg/kg I.M. + xylazine @ 1.5 mg/kg I.M. + propofol I.V. + anaesthetic ether.

The plasma glucose showed significant increase ($P<0.05$) from 1 to 3 hours in treatment I, 1 to 6 hours in treatment II and at 1 hour in treatment III. The control values of 85.6 ± 5.89, 75.4 ± 6.90 and 79.0 ± 11.14 mg/dl increased to maximum values of 120.5 ± 12.7, 124.7 ± 12.77 and 158.4 ± 27.77 mg/dl at 1 hour in treatments I, II and III respectively. This was followed by gradual decrease and at 72 hours post treatment, the values reached near to control values in all the three treatments.

Plasma protein

Changes in plasma protein (gm/dl) level after the different treatments are depicted in table 14.

A non significant change in the values of total protein was observed in all the three treatments. The values ranged between 5.8 ± 0.27 to 6.6 ± 0.21, 5.8 ± 0.37 to 6.4 ± 0.29 and 5.7 ± 0.15 to 6.6 ± 0.32 gm/dl in treatments I, II and III respectively.

Plasma alanine aminotransferase (ALT: L alanine : 2 Oxoglutarate aminotransferase: EC 2.6.1.2)

Changes in the activity of ALT (IU/L) after different treatments are presented in table 15.

A gradual non significant increase in the activity of ALT was observed with maximum values of 22.8 ± 4.75, 34.7 ± 6.39 and 25.0 ± 4.10 IU/ L from control values of 19.7 ± 2.96, 27.8 ± 5.21 and 18.9 ± 2.51 IU/L at 1, 3 and 9 hours in treatments I, II and III respectively. Thereafter, the level fluctuated between 20.3 ± 5.50 to 23.5 ± 4.56, 21.7 ± 2.85 to 32.2. ± 6.97 and 21.7 ± 3.30 to 22.4 ± 4.56 IU/ L in treatments I, II and III respectively.

Table 16 : Mean values (±SE) of Plasma Alkaline Phosphatase (IU/L) at different time intervals following three treatments in dogs.

Time (Hours)	Treatment – I	Treatment – II	Treatment – III
0	213.2 ± 24.1	223.8 ± 20.8	242.3 ± 11.3
1	213.1 ± 25.5	230.5 ±22.5	251.9 ± 12.7
3	211.8 ± 26.8	233.8 ± 21.1	259.8 ± 14.7
6	222.6 ± 28.0	249.0 ±18.8	256.9 ± 10.6
9	251.5 ± 38.6	269.6 ± 23.5	252.1 ± 7.8
24	232.7 ± 48.3	252.1 ± 19.7	225.5 ± 12.7
48	233.8 ± 31.5	206.7 ± 25.7	223.7 ± 11.4
72	231.5 ± 27.6	214.8 ± 25.9	220.1 ± 13.2

Treatments :

I Atropine sulphate @ 0.05 mg/kg I.M. + trifluprom azine hydrochloride @ 1mg/kg I.V. + propofol I.V. + anaesthetic ether.

II Atropine sulphate @ 0.05 mg/kg I.M. + diazepam @ 2 mg/kg I.V. + propofol I.V. + anaesthetic ether.

III Atropine sulphate @ 0.05 mg/kg I.M. + xylazine @ 1.5 mg/kg I.M. + propofol I.V. + anaesthetic ether.

Table 17 : Mean values (±SE) of Plasma Urea Nitrogen (mg/dl) at different time intervals following three treatments in dogs.

Time (Hours)	Treatment – I	Treatment – II	Treatment – III
0	7.2 ± 1.10	9.4 ± 2.03	7.1 ± 1.04
1	9.8 ±1.23	12.5 ± 2.17	11.3 ± 1.72
3	11.5 ± 1.79	12.6 ± 2.10	11.4 ± 1.45
6	13.8 ± 1.67	12.9 ± 1.34	16.7 ± 2.99
9	11.9 ± 1.39	13.1 ± 1.70	17.0 ± 2.60
24	8.4 ± 1.03	11.4 ± 3.41	9.0 ± 1.08
48	8.0 ±1.13	9.8 ± 2.52	7.7 ± 0.82
72	7.0 ± 1.30	8.1 ±1.11	7.5 ± 0.57

Treatments :

I Atropine sulphate @ 0.05 mg/kg I.M. + trifluprom azine hydrochloride @ 1mg/kg I.V. + propofol I.V. + anaesthetic ether.

II Atropine sulphate @ 0.05 mg/kg I.M. + diazepam @ 2 mg/kg I.V. + propofol I.V. + anaesthetic ether.

III Atropine sulphate @ 0.05 mg/kg I.M. + xylazine @ 1.5 mg/kg I.M. + propofol I.V. + anaesthetic ether.

Plasma alkaline phosphatase (ALP: Ortho phosphoric monoester phosphohydrolase: EC 3.1.3.1)

Variations in the activity of plasma alkaline phosphatase (IU/L) after different treatments are shown in table 16.

The activity of plasma alkaline phosphatase increased non significantly in all the three treatments. In treatment I, the maximum level of 251.5 ± 38.6 from control value of 213.2 ±24.1 IU/L at 9 hours, in treatment II, maximum value of 269.6 ±23.5 from control value of 223.8 ± 20.8 IU/L at 9 hours and in treatment III, maximum value of 259.8 ± 14.7 from control value of 242.3 ± 11.3 at 3 hours, were recorded. After maximum rise the values declined gradually and reached near to pre administration level at 72 hours post treatments.

Plasma urea nitrogen

Changes in the level of plasma urea nitrogen (mg/dl) after different treatments are shown in table 17.

A non significant increase was recorded in the level of plasma urea nitrogen in all the three treatments. In treatment I, maximum elevated value of 13.8 ± 1.67 mg/dl from control value of 7.2 ± 1.10 was observed at 6 hours, whereas in treatments II and III, the control values of 9.4 ± 2.03 and 7.1 ± 1.04 increased to maximum values of 13.1 ± 1.70 and 17.0 ± 2.60 mg/dl respectively at 9 hours post treatment. Thereafter, the values decreased gradually in all the three treatments and at 72 hours were observed near to the control values.

Table 18 : Mean values (±SE) of Plasma Creatinine (mg/dl) at different time intervals following three treatments in dogs.

Time (Hours)	Treatment – I	Treatment – II	Treatment – III
0	0.91 ± 0.19	0.55 ± 0.05	0.76 ± 0.16
1	1.01 ± 0.20	0.50 ± 0.06	0.70 ± 0.08
3	0.83 ± 0.20	0.55 ± 0.04	0.63 ± 0.08
6	0.88 ± 0.17	0.60 ± 0.10	0.81 ±0.13
9	0.80 ± 0.18	0.55 ± 0.08	0.66 ± 0.09
24	0.80 ± 0.20	0.51 ± 0.06	0.58 ± 0.08
48	0.68 ± 0.04	0.66 ± 0.07	0.60 ± 0.07
72	0.54 ± 0.05	0.56 ± 0.06	0.66 ± 0.06

Treatments :

I Atropine sulphate @ 0.05 mg/kg I.M. + triflupromazine hydrochloride @ 1mg/kg I.V. + propofol I.V. + anaesthetic ether.

II Atropine sulphate @ 0.05 mg/kg I.M. + diazepam @ 2 mg/kg I.V. + propofol I.V. + anaesthetic ether.

III Atropine sulphate @ 0.05 mg/kg I.M. + xylazine @ 1.5 mg/kg I.M. + propofol I.V. + anaesthetic ether.

Plasma creatinine

The average values of plasma creatinine (mg/dl) are listed in table 18.

A non significant variation in the content of plasma creatinine was observed in all the three treatments at various intervals. The values ranged between 0.54 ± 0.05 to 1.01 ± 0.20, 0.50 ± 0.06 to 0.66 ± 0.07 and 0.58 ± 0.08 to 0.81 ± 0.13 mg /dl in treatments I, II and III respectively.

~~~ Discussion

DISCUSSION

In this era of advancement introduction of modern techniques and new drugs are going on. This makes the anaesthesiologist to use more reliable, efficient and superior anaesthetic techniques and drugs to approach the target. The successful outcome of any surgery depends on particular regime used by anaesthesiologist.

The responses of new general anaesthetic drug or its combinations must be evaluated before clinical implementation to assess its effect on liver and kidney functions and various haematological attributes. The variations in response to the drug may be due to individual variation and use of different drug combinations. Therefore, it becomes essential that characteristics of drug should be considered before recommending a drug for use in clinical practice.

Response to pain stimuli, safe recovery from anaesthesia, variations in cardiovascular and respiratory function, alteration in liver and kidney functions are the few methods employed to evaluate the efficiency and superiority of new anaesthetic drugs over the traditional one.

The present investigations were primarily designed to elucidate the extent of clinical, haematological and biochemical variation in response to anaesthesia, induced by using propofol and anesthetic ether in combination with preanaesthetics, such as triflupromazine hydrochloride, diazepam or xylazine in dogs.

A. CLINICAL STUDIES

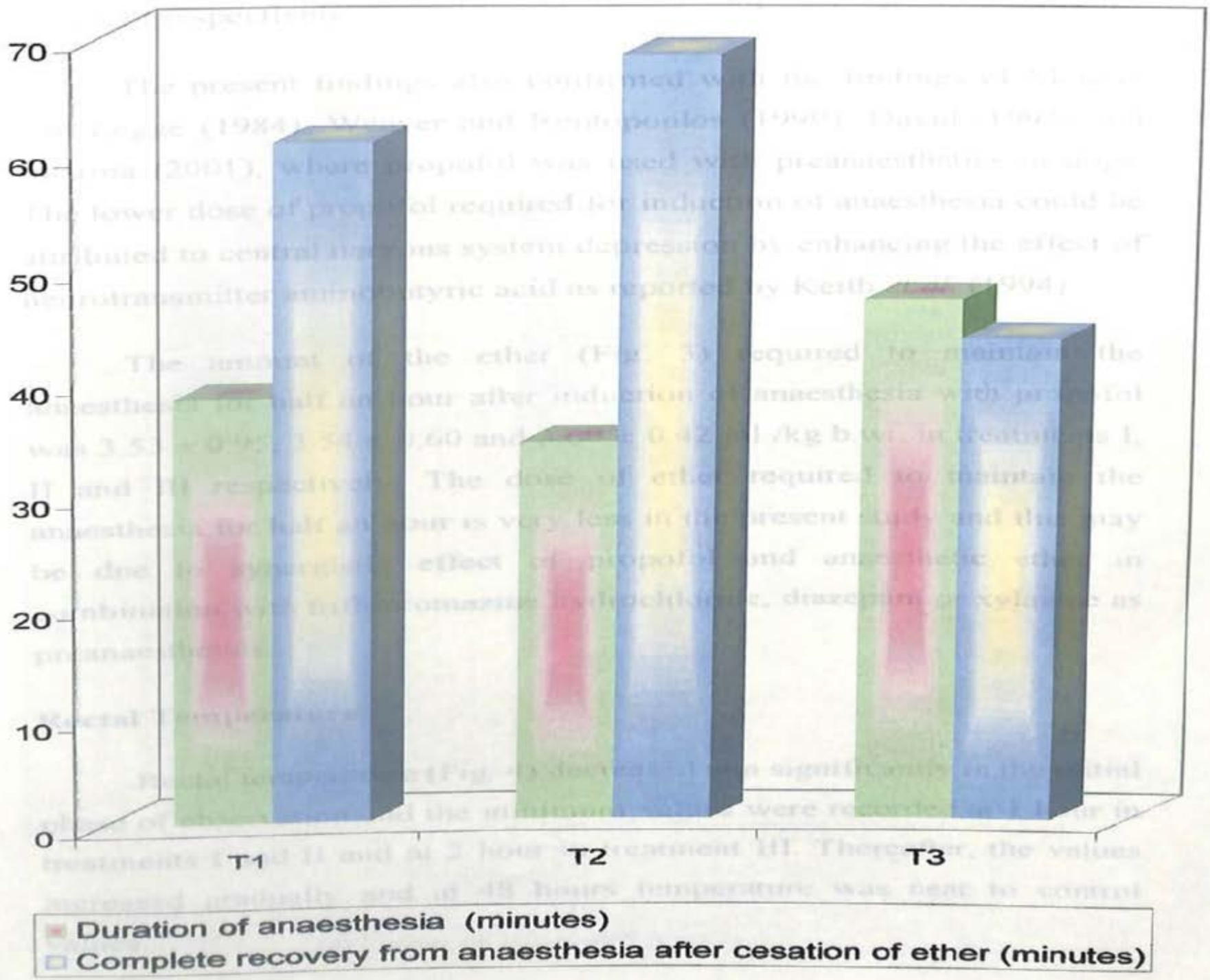
The duration of surgical anaesthesia was 38.33 ± 4.40, 34.16 ± 1.35 and 46.83 ± 5.32 minutes, whereas complete recovery from anaesthesia was in 60.83 ± 18.40, 68.33 ± 22.45 and 43.33 ± 9.54 minutes in treatments I, II and III respectively (Fig. 1).

The sequence of symptoms leading to loss of reflexes as well as event of recovery in animals belonging to treatments I, II and III confirm neuromuscular block as reported by Hall (1978). Morgan and Legge (1989) recorded duration of anaesthesia 2.52 to 9.4 minutes with propofol alone or in combination with preanaesthtic in dogs, whereas David (1993) reported duration of propofol anaesthesia for 7.30 minutes. Similarly, Sharma *et al.* (2001) recorded duration of surgical anaesthesia between 6.66 ± 0.55 to 34.83 ± 1.49 minutes with single or repeated administration of propofol in combination with triflupromazine and midazolam as preanaesthetics.

Morgan and Legge (1989) and Weaver and Reptopoulos (1990) recorded complete recovery within 24 to 40 and 16.42 to 40.4 minutes respectively with propofol alone and in combination with preanaesthetics in dogs. Whereas, Sharma *et al.* (2001) recorded complete recovery from anaesthesia in 63.83 ± 23.05 to 322 ± 59.79 minutes with single or repeated administration of propofol with preanaesthetics.

The longer duration of anaesthesia observed with treatments I, II and III in the present study may be due to continuous administration of ether for 30 minutes after induction with propofol. The recovery from the anaesthesia started within 5 to 10 minutes after cessation of ether inhalation.

FIG. 1: DURATION OF ANAESTHESIA AND COMPLETE RECOVERY AFTER ADMINISTRATION OF PROPOFOL AND ANAESTHETIC ETHER IN COMBINATION WITH PREANAESTHETICS IN DOGS



The complete recovery from anaesthesia was also faster in the present study and may be due to the fact that ether is almost entirely eliminated from the body through the lungs (Hall and Clarke, 1983).

The dose of propofol (Fig. 2) used to provide surgical anaesthesia was 4.28 ±0.47, 4.41 ±0.40 and 2.82 ± 0.62 mg/kg b. wt. in treatments I, II and III respectively.

The present findings also confirmed with the findings of Morgan and Legge (1984); Weaver and Reptopoulos (1990); David (1993) and Sharma (2001), where propofol was used with preanaesthetics in dogs. The lower dose of propofol required for induction of anaesthesia could be attributed to central nervous system depression by enhancing the effect of neurotransmitter aminobutyric acid as reported by Keith *et al.* (1994).

The amount of the ether (Fig. 3) required to maintain the anaesthesia for half an hour after induction of anaesthesia with propofol was 3.53 ± 0.95, 3.54 ± 0.60 and 3.60 ± 0.42 ml /kg b.wt. in treatments I, II and III respectively. The dose of ether required to maintain the anaesthesia for half an hour is very less in the present study and this may be due to synergistic effect of propofol and anaesthetic ether in combination with triflupromazine hydrochloride, diazepam or xylazine as preanaesthetics.

Rectal Temperature

Rectal temperature (Fig. 4) decreased non significantly in the initial phase of observation and the minimum values were recorded at 1 hour in treatments I and II and at 2 hour in treatment III. Thereafter, the values increased gradually and at 48 hours temperature was near to control values.

FIG. 2 : DOSE OF PROPOFOL AFTER ADMINISTRATION OF PROPOFOL AND ANAESTHETIC ETHER IN COMBINATION WITH PREANAESTHETICS IN DOGS

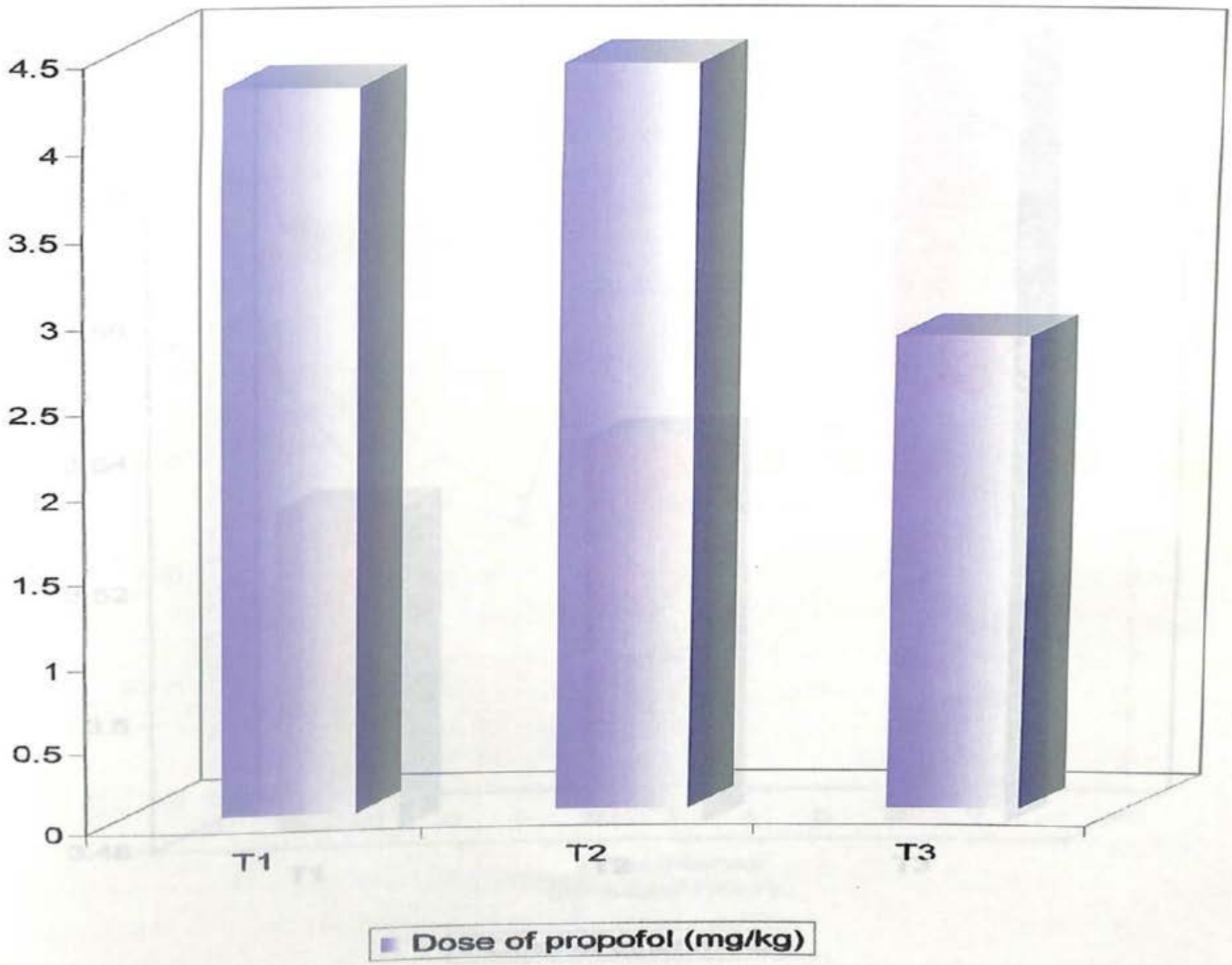


FIG. 3 : DOSE OF ETHER AFTER ADMINISTRATION OF PROPOFOL AND ANAESTHETIC ETHER IN COMBINATION WITH PREANAESTHETICS IN DOGS

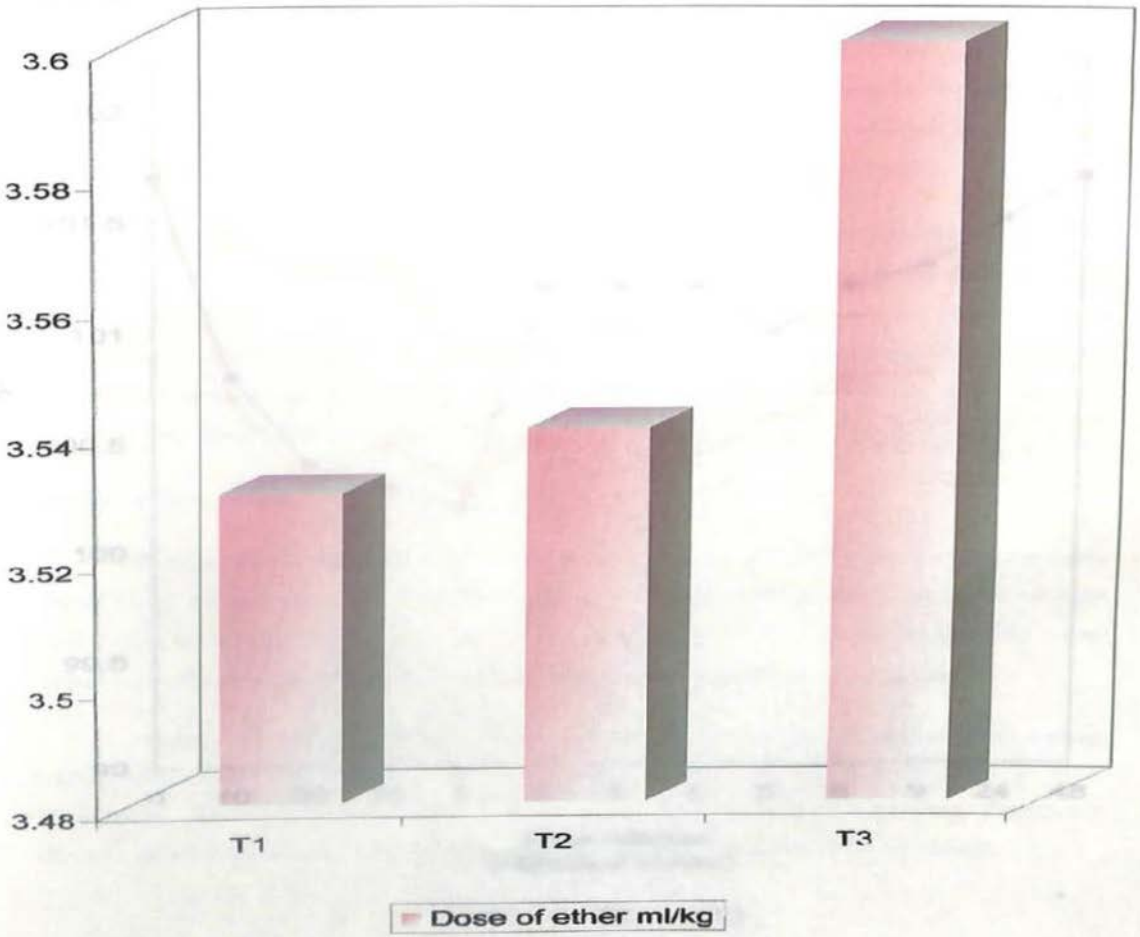


FIG. 3 : DOSE OF ETHER AFTER ADMINISTRATION OF PROPOFOL AND ANAESTHETIC ETHER IN COMBINATION WITH PREANAESTHETICS IN DOGS

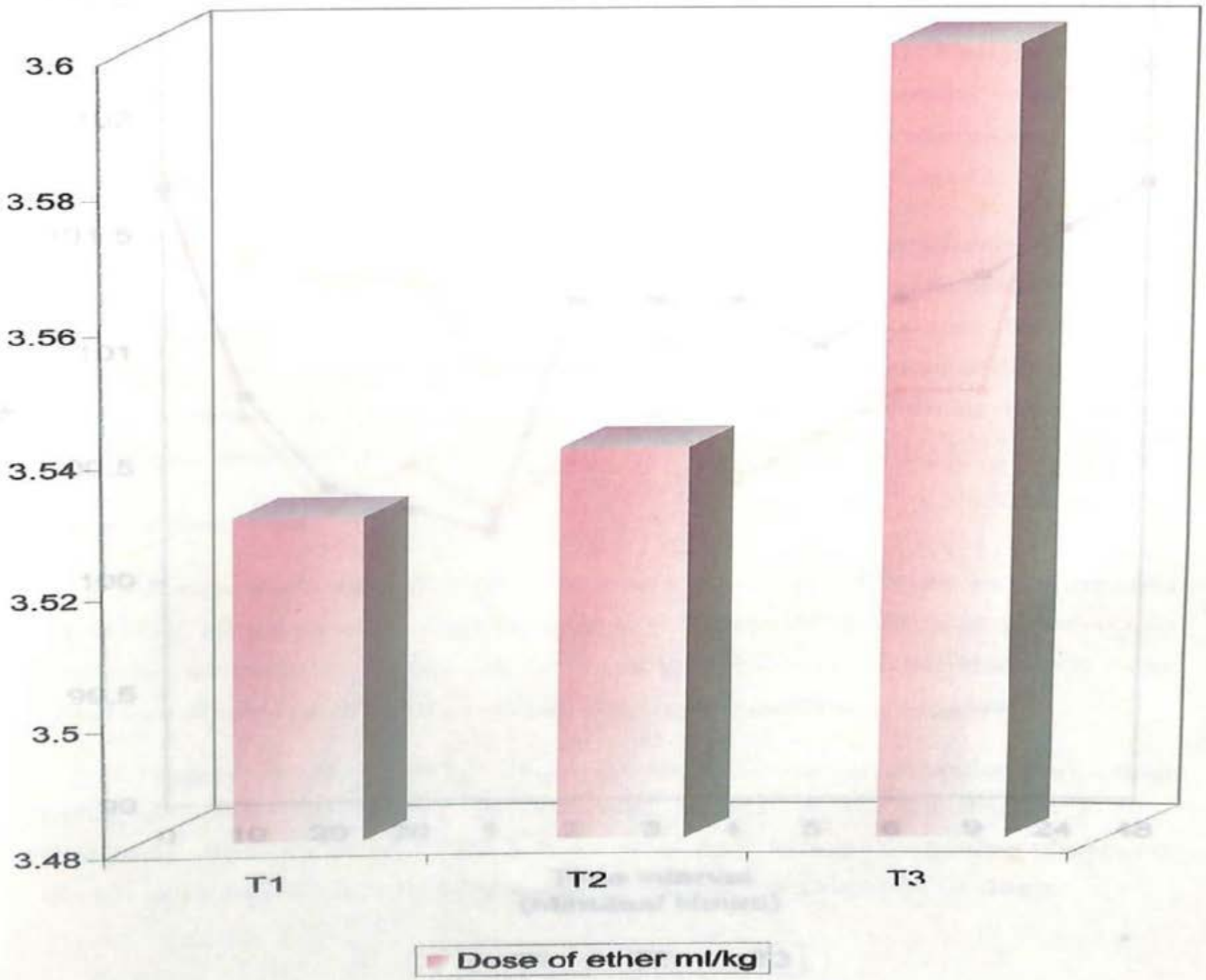
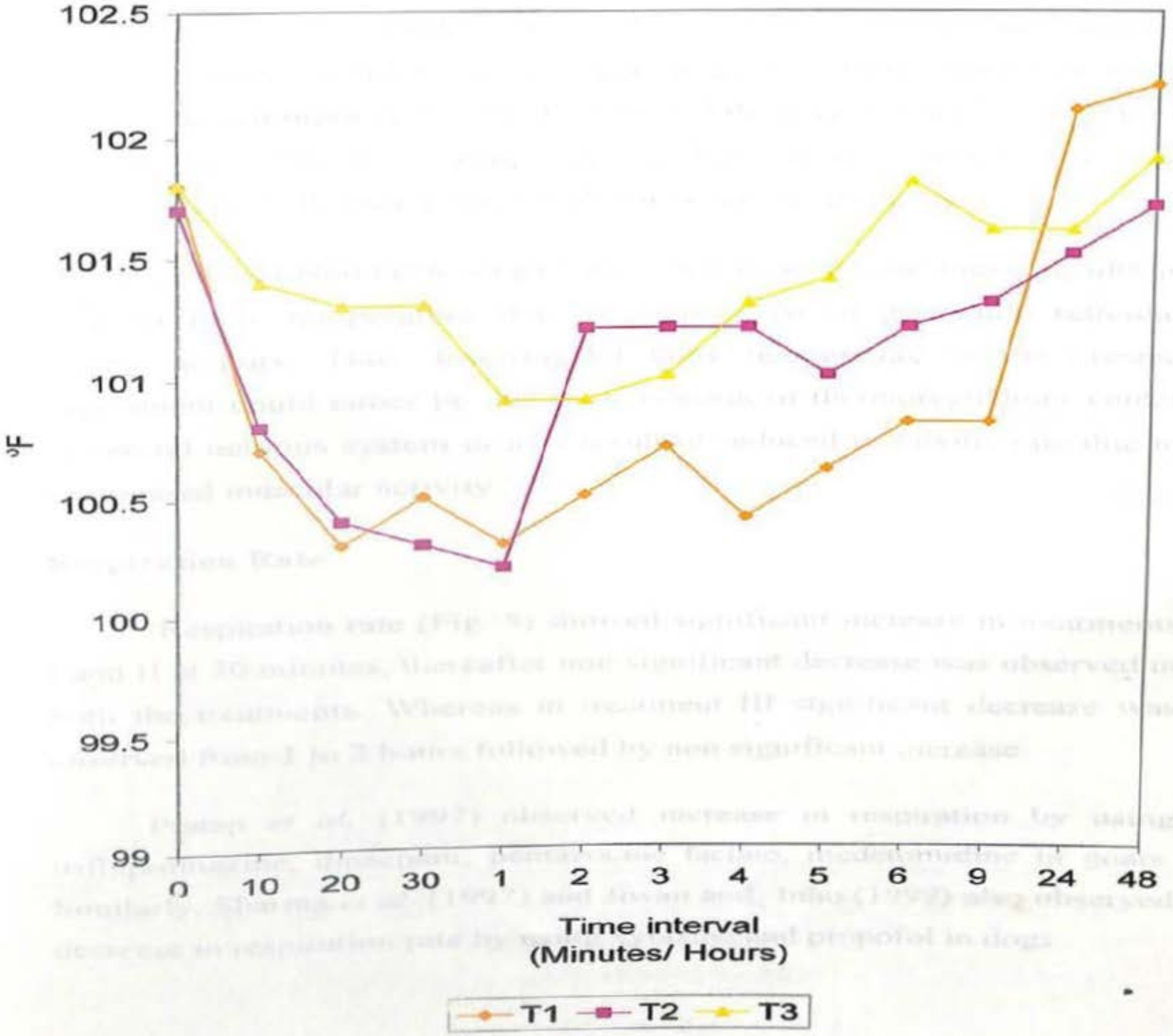


FIG. 4 : TEMPERATURE AFTER ADMINISTRATION OF PROPOFOL AND ANAESTHETIC ETHER IN COMBINATION WITH PREANAESTHETICS IN DOGS



David *et al.* (1993) observed decrease in body temperature by using propofol with triflupromazine in dogs. Thurman *et al.* (1995) and England *et al.* (1996) observed non significant change in rectal temperature by using propofol, whereas Venugopalan *et al.* (2002) recorded significant decrease in rectal temperature by using propofol-ketamine anaesthesia in dogs. Decrease in temperature was also observed by using propofol and xylazine (Jiwan and Inho, 1999). Rangnath *et al.* (1992) and Niranjan *et al.* (1994) observed decrease in rectal temperature by using buprinorphine, triflupromazine, barbiturate combination in dogs and ketamine-triflupromazine combination in cats respectively.

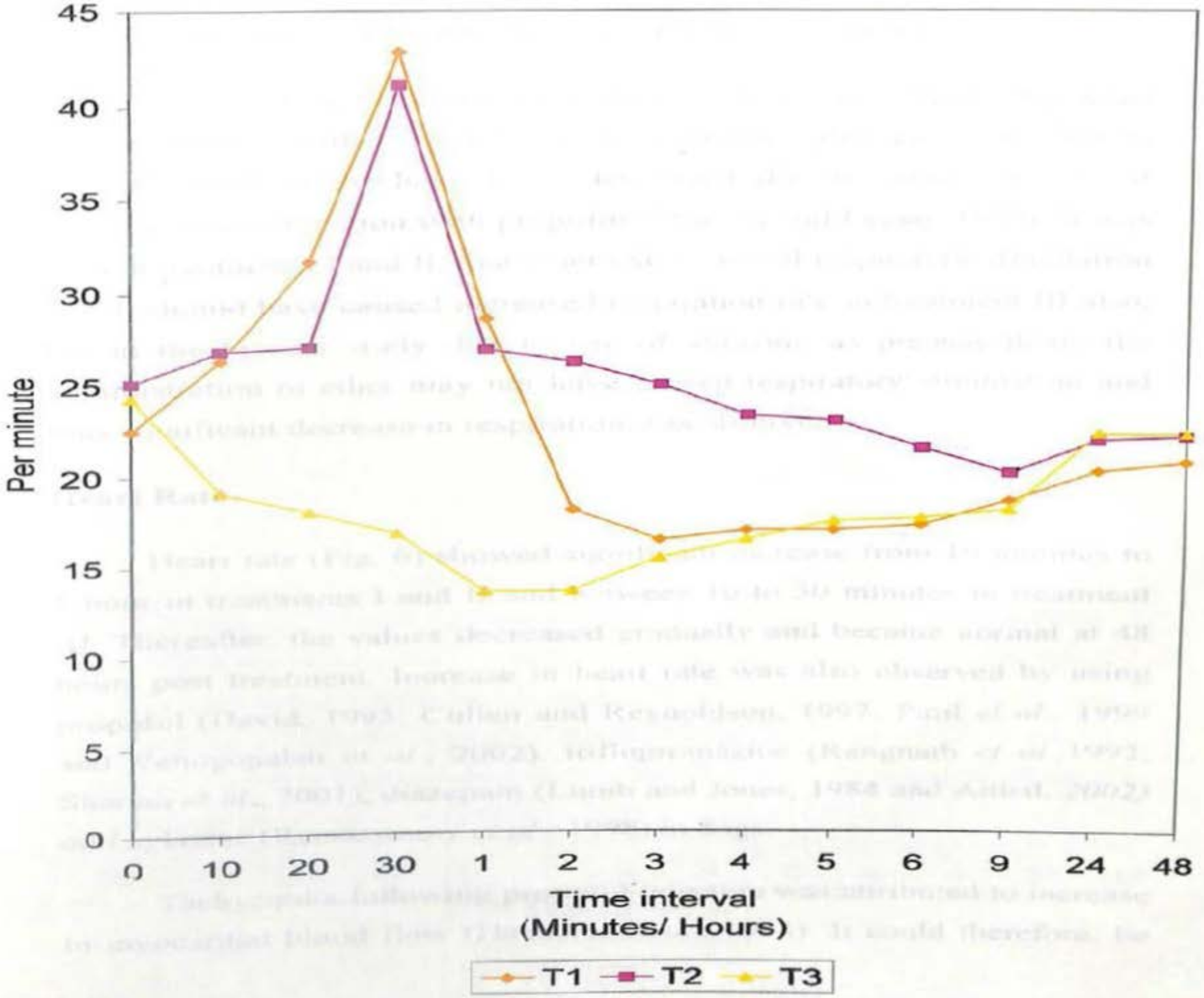
Keel and Neil (1965) mentioned that general anaesthesia results in drop of body temperature due to suppression of ascending reticular system activity. Thus, lowering of body temperature in the present experiment could either be due to depression of thermoregulatory center of central nervous system or as a result of reduced metabolic rate due to suppressed muscular activity.

Respiration Rate

Respiration rate (Fig. 5) showed significant increase in treatments I and II at 30 minutes, thereafter non significant decrease was observed in both the treatments. Whereas in treatment III significant decrease was observed from 1 to 2 hours followed by non significant increase.

Pratap *et al.* (1997) observed increase in respiration by using triflupromazine, diazepam, pentazocine lactate, medetomidine in goats. Similarly, Sharma *et al.* (1997) and Jiwan and Inho (1999) also observed decrease in respiration rate by using xylazine and propofol in dogs.

FIG. 5: RESPIRATION RATE AFTER ADMINISTRATION OF PROPOFOL AND ANAESTHETIC ETHER IN COMBINATION WITH PREANAESTHETICS IN DOGS



The significant increase in the respiration rate in treatments I and II could be attributed to initial respiratory stimulating effect of diethyl ether (Hall and Clarke, 1983; Vickers *et al.*, 1984). This is followed by depression in the deepest plane of surgical anaesthesia, which may be responsible for decrease in respiration rate as also observed in the later stage of anaesthesia in treatments I and II in the present study.

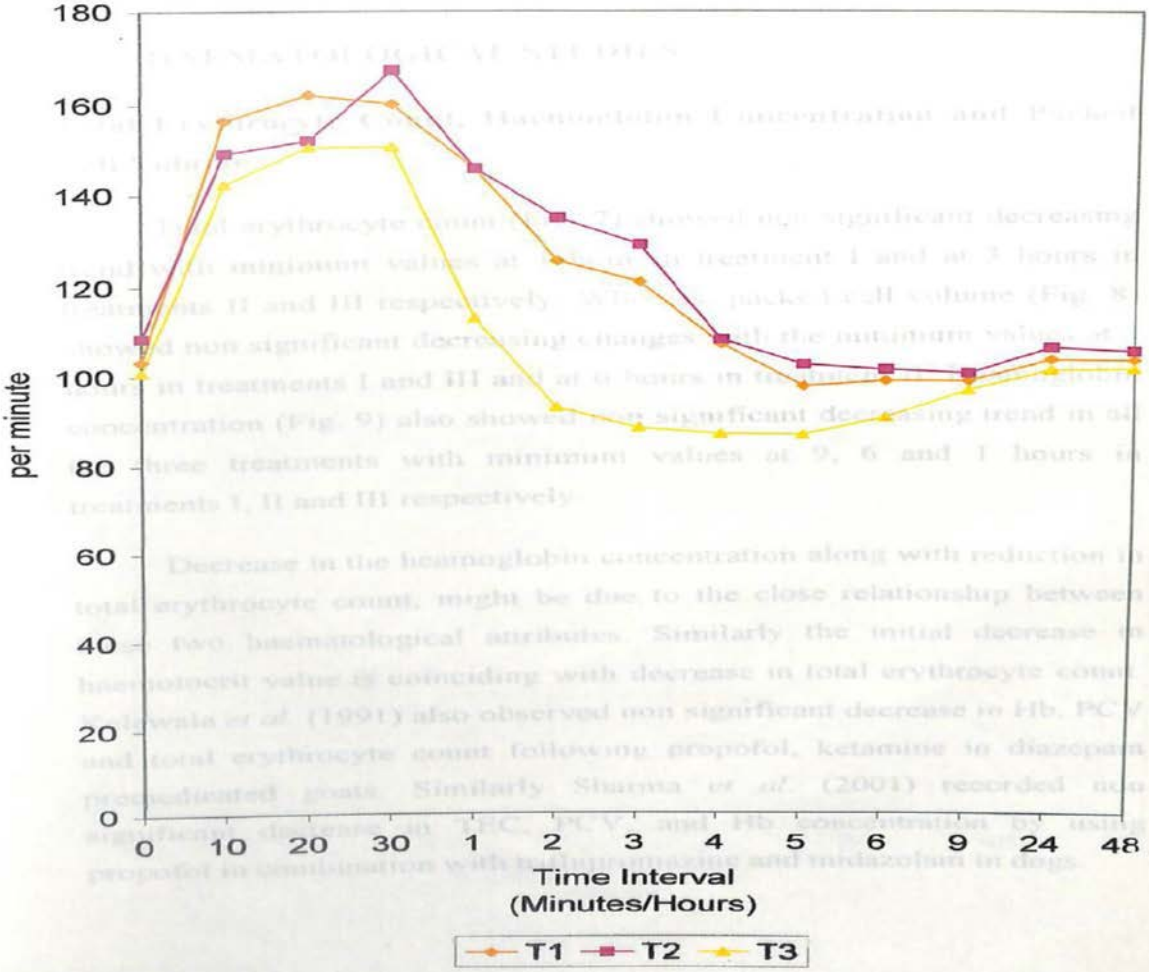
The significant decrease in treatment III, where xylazine was used in combination with propofol and anaesthethic ether might be due to aponea which might have been developed due to administration of xylazine in combination with propofol (Morgan and Legge, 1989). It was seen in treatments I and II, that ether causes initial respiratory stimulation which should have caused increased respiration rate in treatment III also, but in the present study due to use of xylazine as preanaesthetic the administration of ether may not have caused respiratory stimulation and thus significant decrease in respiration was observed.

Heart Rate

Heart rate (Fig. 6) showed significant increase from 10 minutes to 1 hour in treatments I and II and between 10 to 30 minutes in treatment III. Thereafter, the values decreased gradually and became normal at 48 hours post treatment. Increase in heart rate was also observed by using propofol (David, 1993; Cullen and Reynoldson, 1997; Patil *et al.*, 1999 and Venugopalan *et al.*, 2002), trifluprom azine (Rangnath *et al.*, 1992; Sharma *et al.*, 2001), diazepam (Lumb and Jones, 1984 and Aithal, *2002) and* xylazine (Ramaswamy *et al.*, 1998) in dogs.

Tachycardia following propofol injection was attributed to increase in myocardial blood flow (Haeberer *et al.*, 1993). It could therefore, be

FIG. 6: HEART RATE AFTER ADMINISTRATION OF PROPOFOL AND ANAESTHETIC ETHER IN COMBINATION WITH PREANAESTHETICS IN DOGS



hypothesized that increase in heart rate in all the three treatments might be due to stimulation of cardio-exitatory centers of brain or stimulation of sympathetic nervous system. Direct stimulation to the CNS as a result of struggling and excitement could be yet another factor responsible for significant increase in heart rate.

B. HAEMATOLOGICAL STUDIES

Total Erythrocyte Count, Haemoglobin Concentration and Packed Cell Volume

Total erythrocyte count (Fig. 7) showed non significant decreasing trend with minimum values at 1 hour in treatment I and at 3 hours in treatments II and III respectively. Whereas, packed cell volume (Fig. 8) showed non significant decreasing changes with the minimum values at 3 hours in treatments I and III and at 6 hours in treatment II. Heamoglobin concentration (Fig. 9) also showed non significant decreasing trend in all the three treatments with minimum values at 9, 6 and 1 hours in treatments I, II and III respectively.

Decrease in the heamoglobin concentration along with reduction in total erythrocyte count, might be due to the close relationship between these two haematological attributes. Similarly the initial decrease in haemotocrit value is coinciding with decrease in total erythrocyte count. Kelawala *et al.* (1991) also observed non significant decrease in Hb, PCV and total erythrocyte count following propofol, ketamine in diazepam premedicated goats. Similarly Sharma *et al.* (2001) recorded non significant decrease in TEC, PCV, and Hb concentration by using propofol in combination with trifluprometazine and midazolam in dogs.

FIG. 7: TOTAL ERYTHROCYTE COUNT AFTER ADMINISTRATION OF PROPOFOL AND ANAESTHETIC ETHER IN COMBINATION WITH PREANAESTHETICS IN DOGS

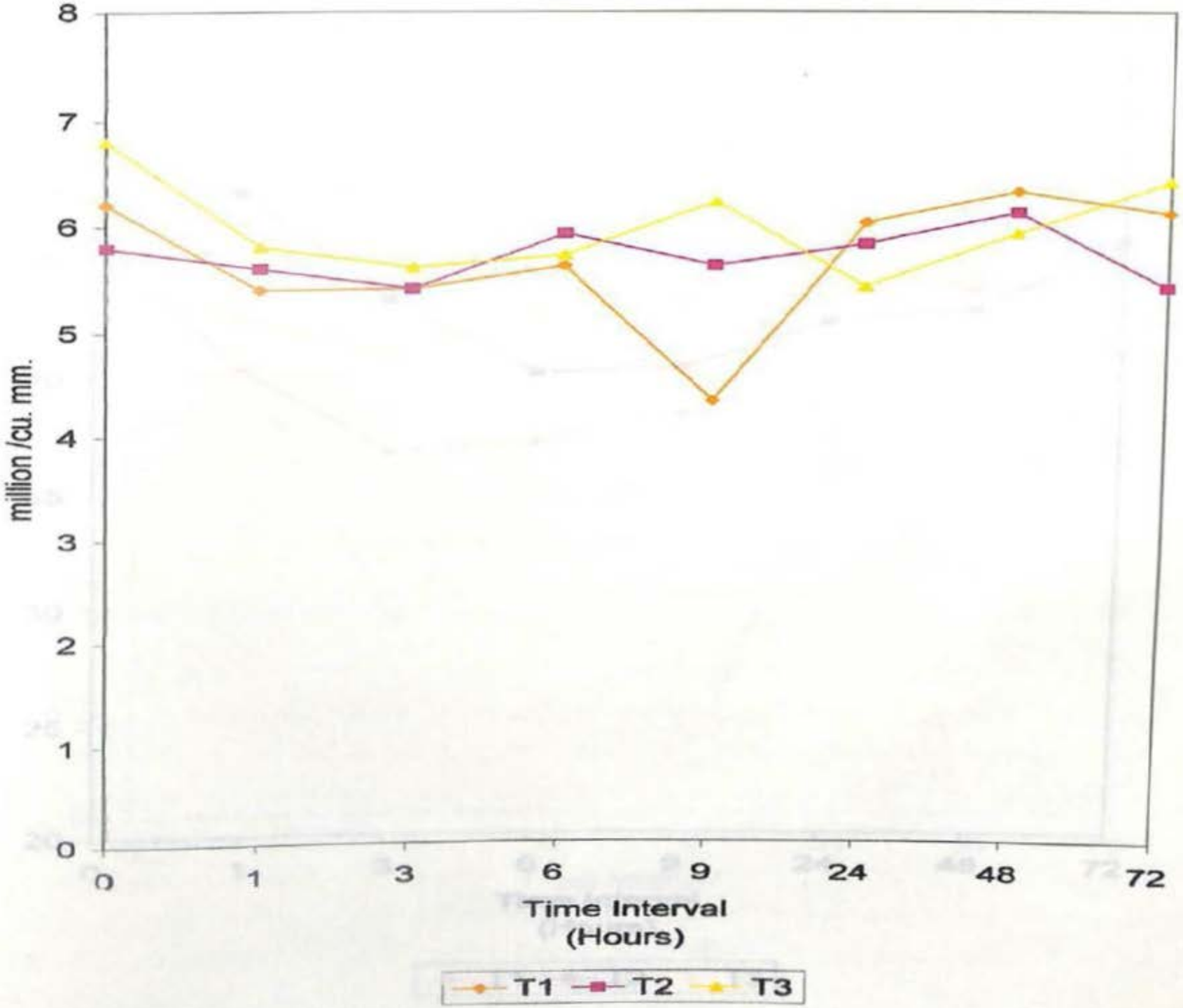


FIG. 8 : PACKED CELL VOLUME AFTER ADMINISTRATION OF PROPOFOL AND ANAESTHETIC ETHER IN COMBINATION WITH PREANAESTHETICS IN DOGS

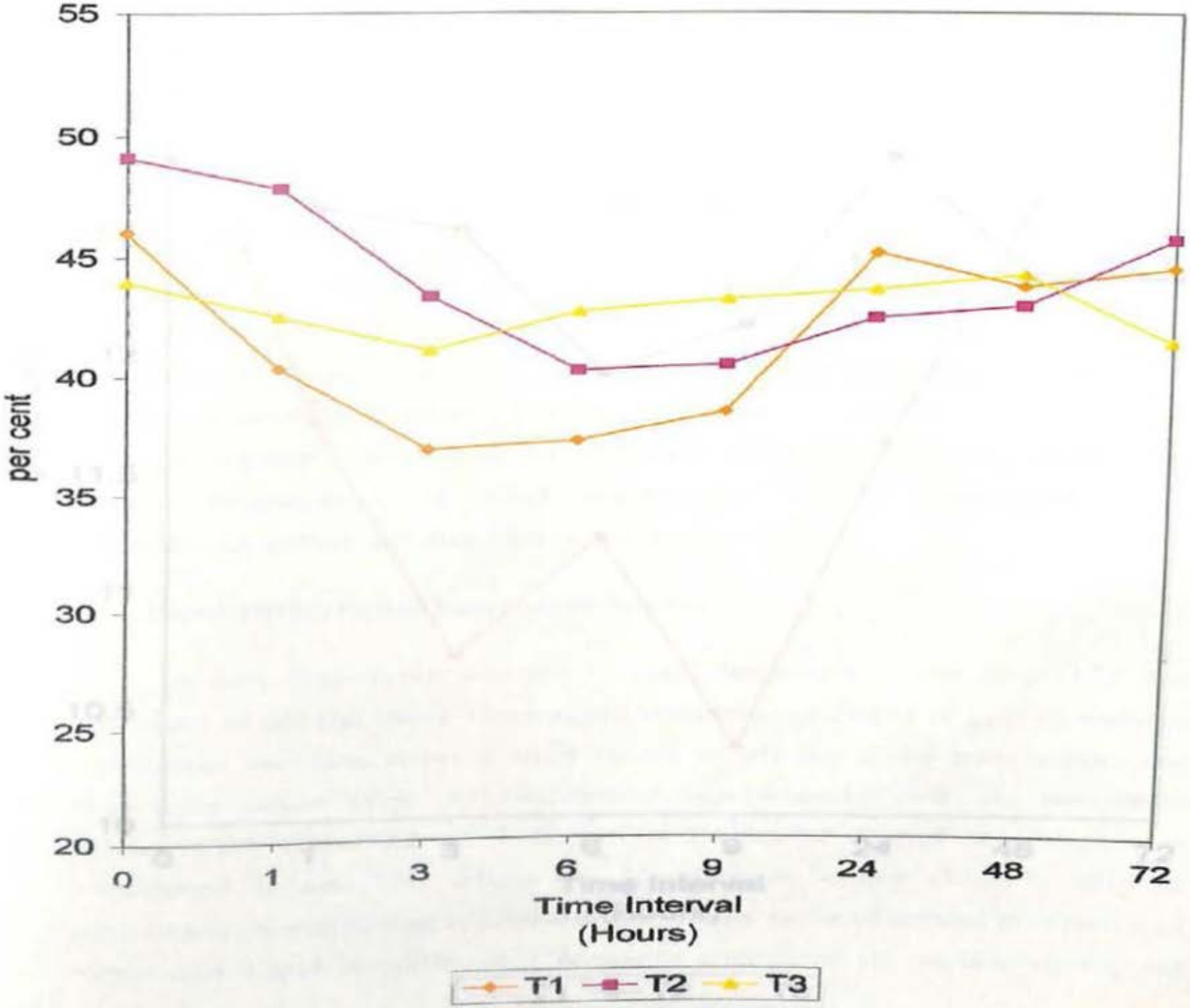
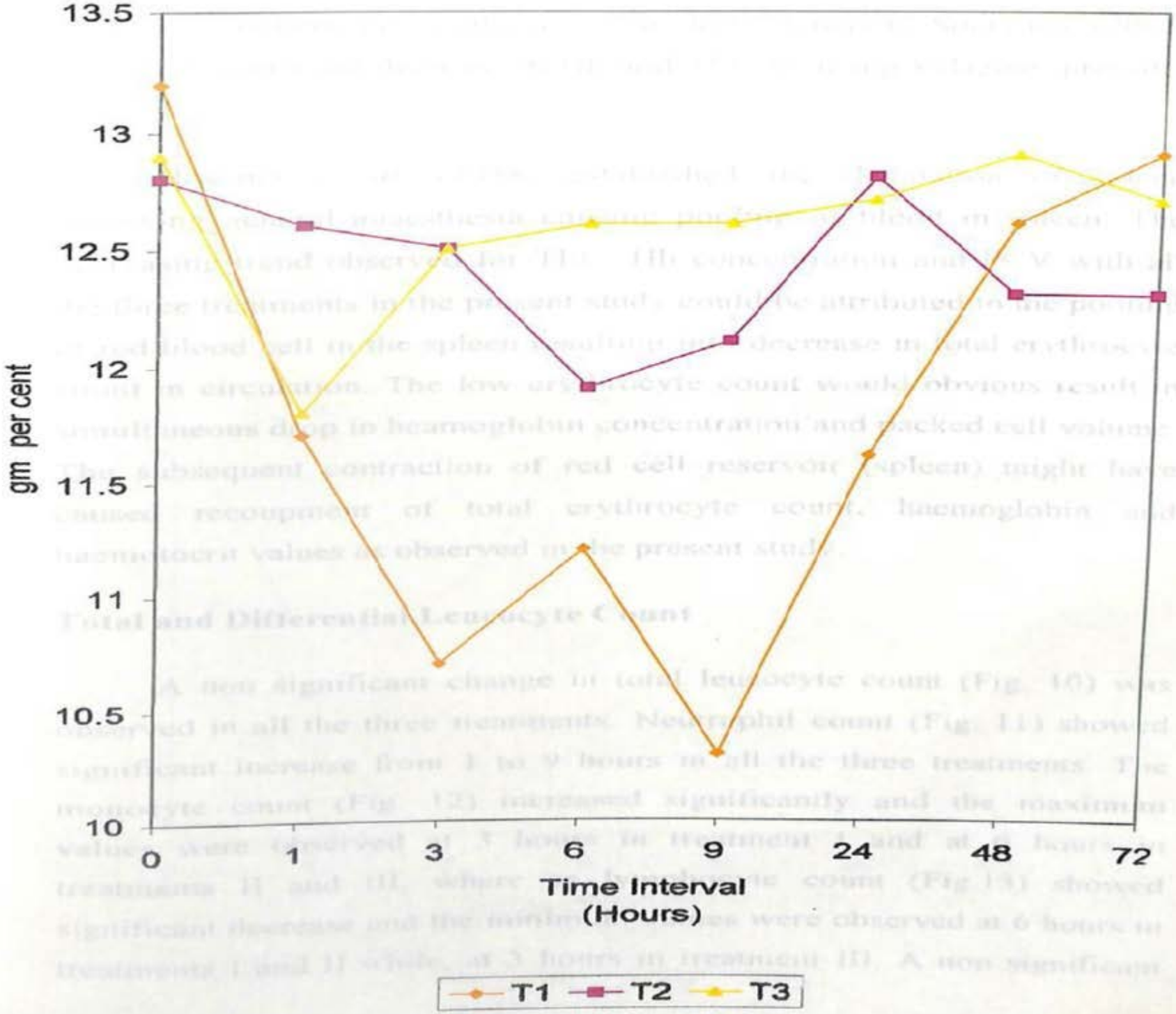


FIG. 9 : HAEMOGLOBIN CONCENTRATION AFTER ADMINISTRATION OF PROPOFOL AND ANAESTHETIC ETHER IN COMBINATION WITH PREANAESTHETICS IN DOGS



Jani *et al.* (1982) observed decrease in PCV and Hb concentration while, Akhare *et al.* (2000) recorded non significant decrease in Hb and TEC with significant decrease in PCV by using atropine-diazepam and diazepam-ketamine combination in dogs and goats respectively. Sharma *et al.* (1983) reported decrease in TEC, Hb and PCV by using xylazine, atropine, thiopentone combination in dogs, whereas Sooryada (2001) recorded significant decrease in Hb and TEC by using xylazine- propofol in dogs.

Housner *et al.* (1938) established the di latation of spleen following general anaesthesia causing pooling of blood in spleen. The decreasing trend observed for TEC, Hb concentration and PCV with all the three treatments in the present study could be attributed to the pooling of red blood cell in the spleen resulting into decrease in total erythrocyte count in circulation. The low erythrocyte count would obvious result in simultaneous drop in heamoglobin concentration and packed cell volume. The subsequent contraction of red cell reservoir (spleen) might have caused recoupment of total erythrocyte count, haemoglobin and haemotocrit values as observed in the present study.

Total and Differential Leucocyte Count

A non significant change in total leucocyte count (Fig. 10) was observed in all the three treatments. Neutrophil count (Fig. 11) showed significant increase from 1 to 9 hours in all the three treatments. The monocyte count (Fig. 12) increased significantly and the maximum values were observed at 3 hours in treatment I and at 6 hours in treatments II and III, where as lymphocyte count (Fig.13) showed significant decrease and the minimum values were observed at 6 hours in treatments I and II while, at 3 hours in treatment III. A non significant

FIG. 10: TOTAL LEUCOCYTE COUNT AFTER ADMINISTRATION OF PROPOFOL AND ANAESTHETIC ETHER IN COMBINATION WITH PREANAESTHETICS IN DOGS

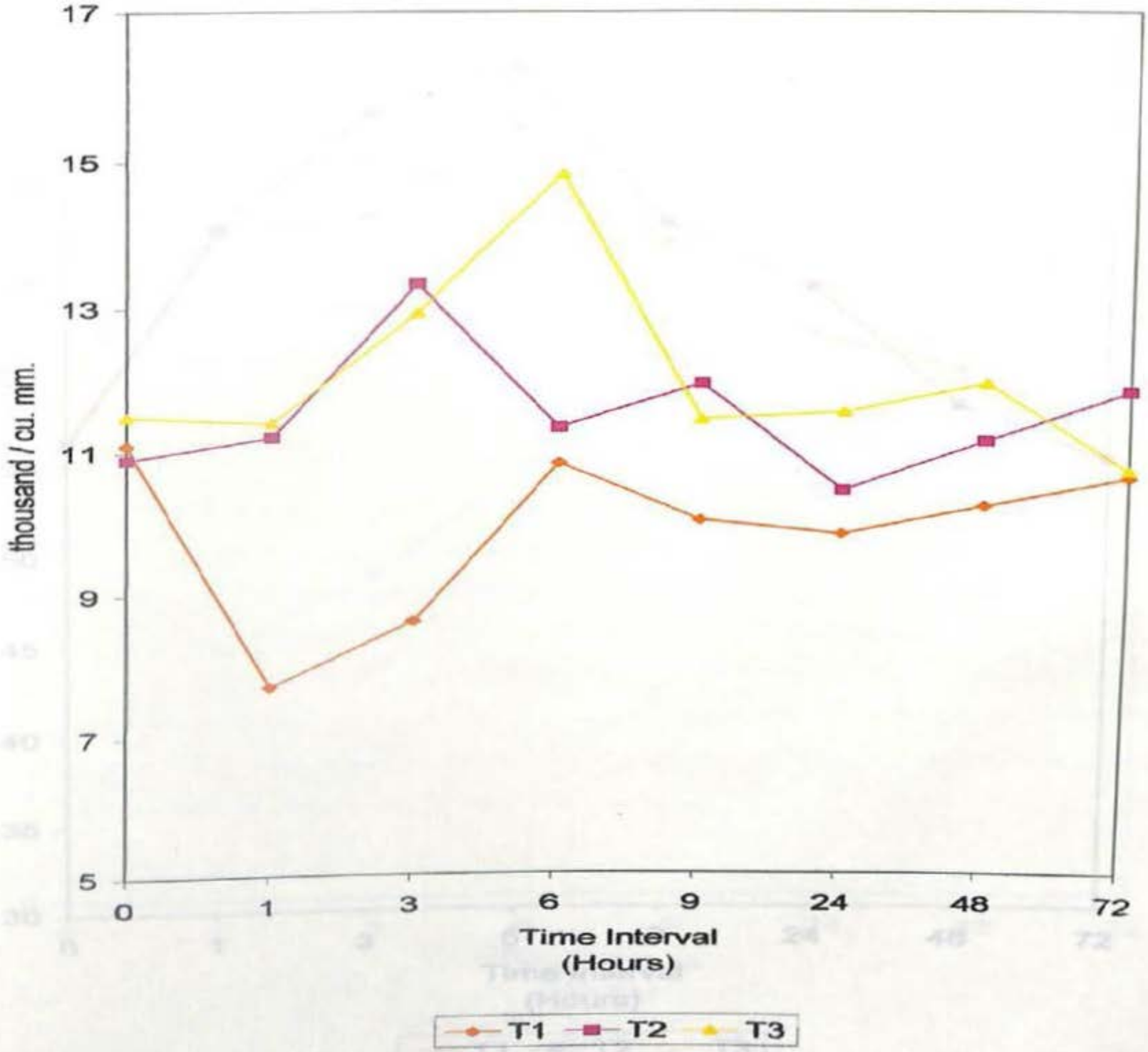


FIG. 11 : NEUTROPHIL COUNT AFTER ADMINISTRATION OF PROPOFOL AND ANAESTHETIC ETHER IN COMBINATION WITH PREANAESTHETICS IN DOGS

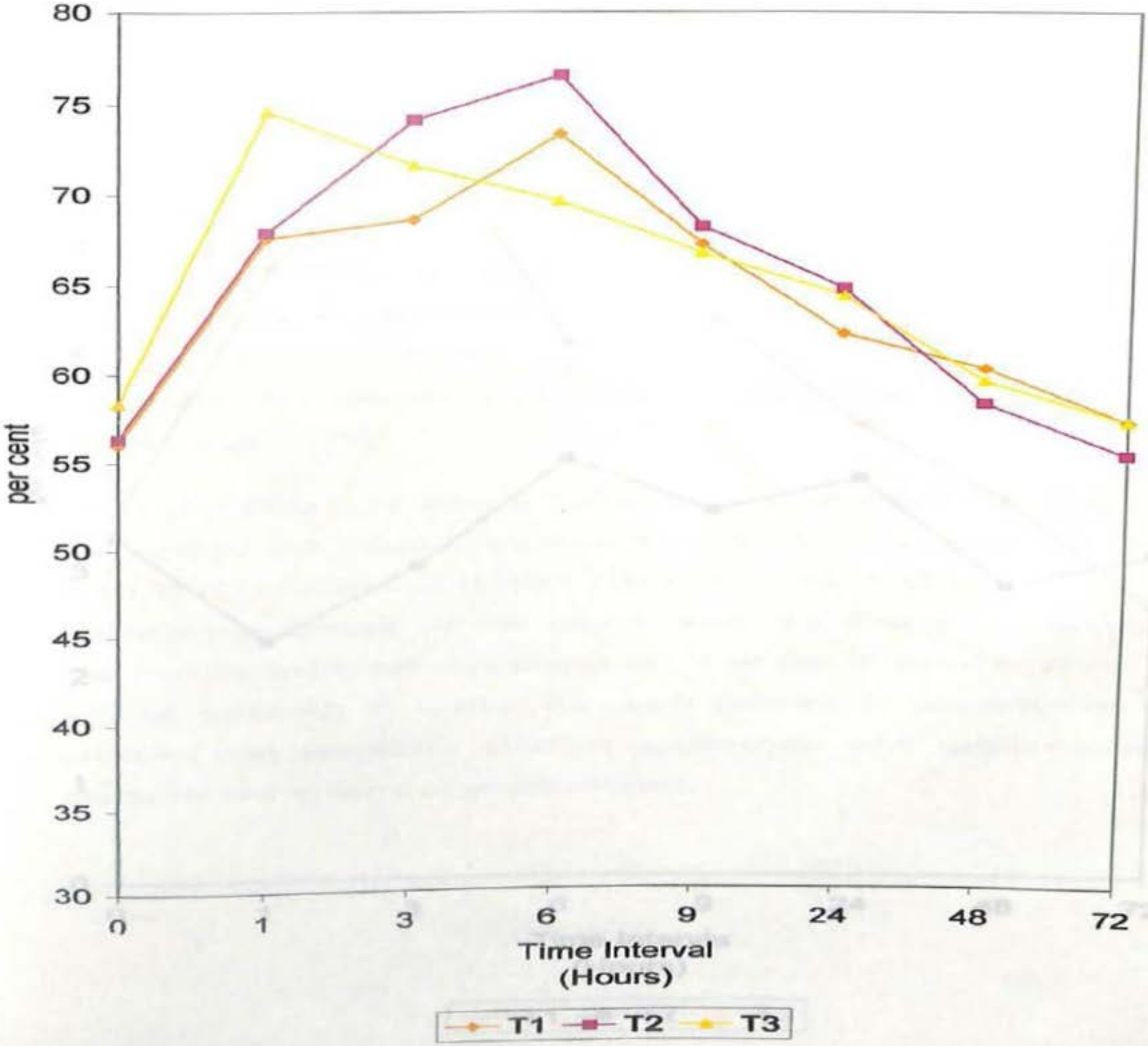
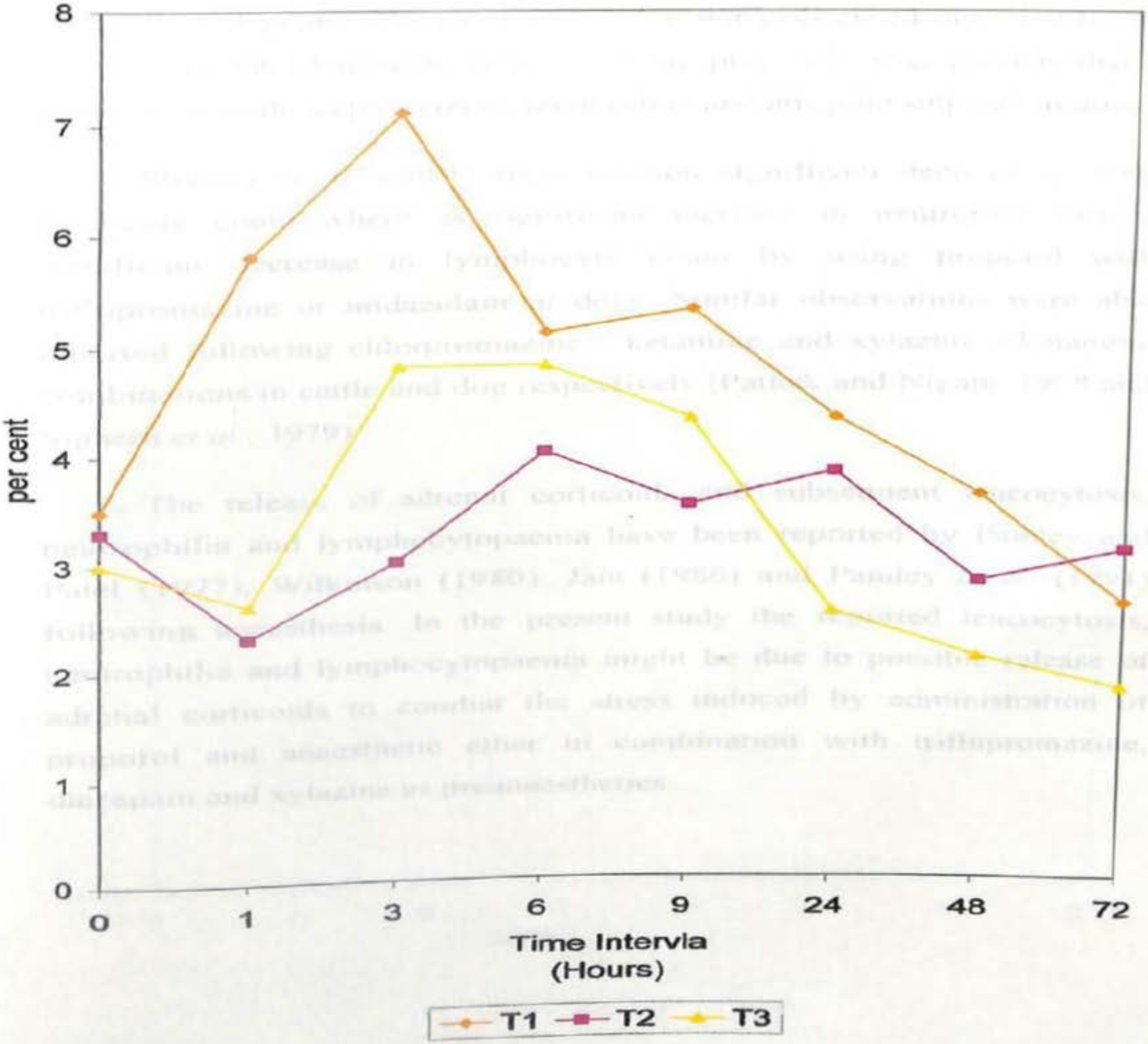


FIG. 12: MONOCYTE COUNT AFTER ADMINISTRATION OF PROPOFOL AND ANAESTHETIC ETHER IN COMBINATION WITH PREANAESTHETICS IN DOGS



difference was observed in eosinophil count (Fig. 14) in all the three treatments.

Kelawala *et al.* (1991) also observed non significant decrease in total leucocyte count by using propofol-ketamine in diazepam premedicated goats, whereas Gill *et al.* (1996) observed non significant decrease in total leucocyte count by using propofol, after preanaesthetic medication with acepromazine, meperidine and atropine sulphate in dogs.

Sharma *et al.* (2001) recorded non significant decrease in total leucocyte count where as significant increase in neutrophil with a significant decrease in lymphocyte count by using propofol with triflupromazine or midazolam in dogs. Similar observations were also reported following chlorpromazine - ketamine and xylazine - ketamine combinations in cattle and dog respectively (Pathak and Nigam, 1978 and Sighera *et al.*, 1979).

The release of adrenal corticoids and subsequent leucocytosis, neutrophilia and lymphocytopaenia have been reported by Pandey and Patel (1977); Wilkinson (1980); Jain (1986) and Pandey *et al.* (1991) following anaesthesia. In the present study the reported leucocytosis, neutrophilia and lymphocytopaenia might be due to possible release of adrenal corticoids to combat the stress induced by administration of propofol and anaesthetic ether in combination with triflupromazine, diazepam and xylazine as preanaesthetics.

FIG. 13 : LYMPHOCYE COUNT AFTER ADMINISTRATION OF PROPOFOL AND ANAESTHETIC ETHER IN COMBINATION WITH PREANAESTHETICS IN DOGS

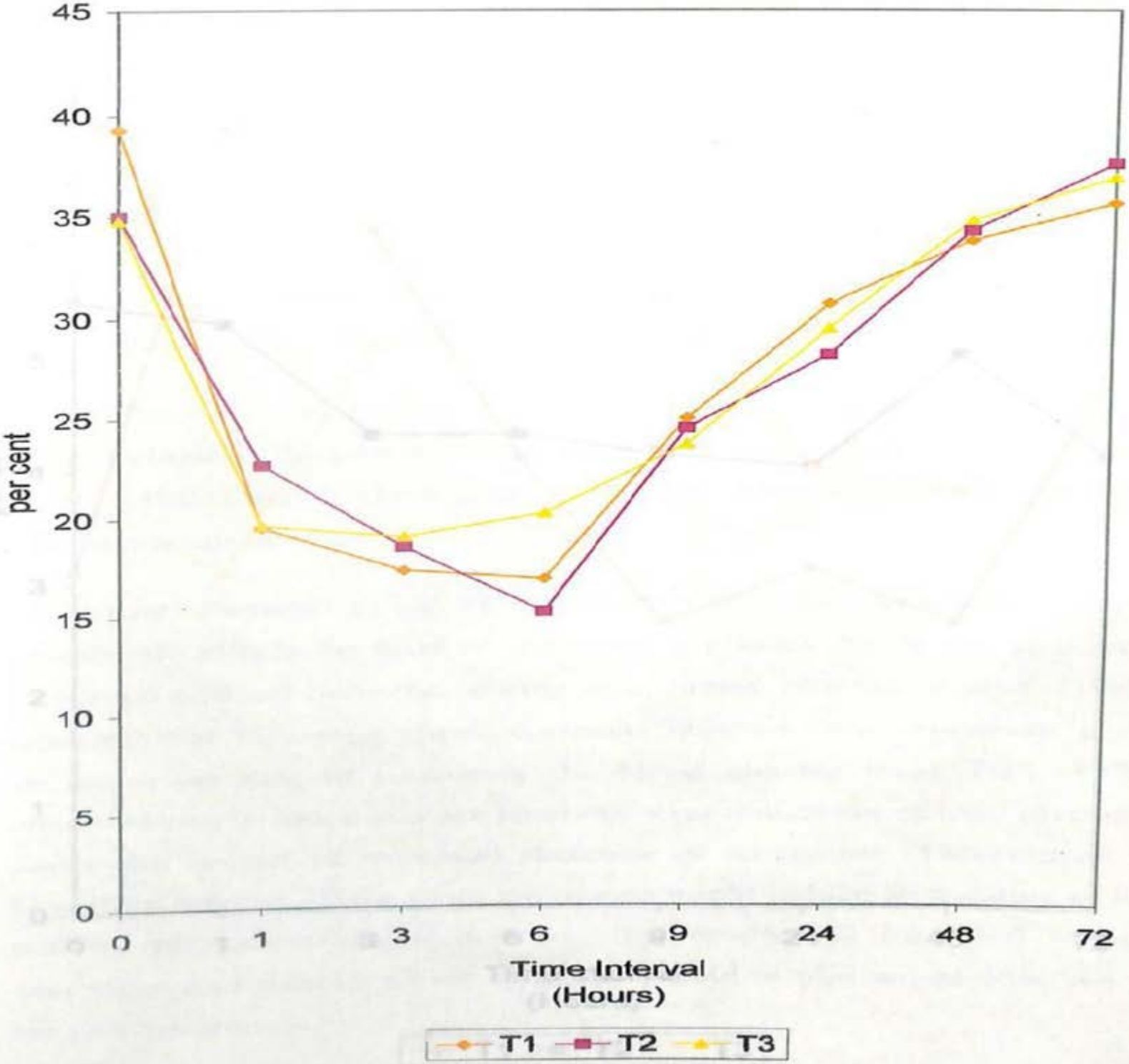
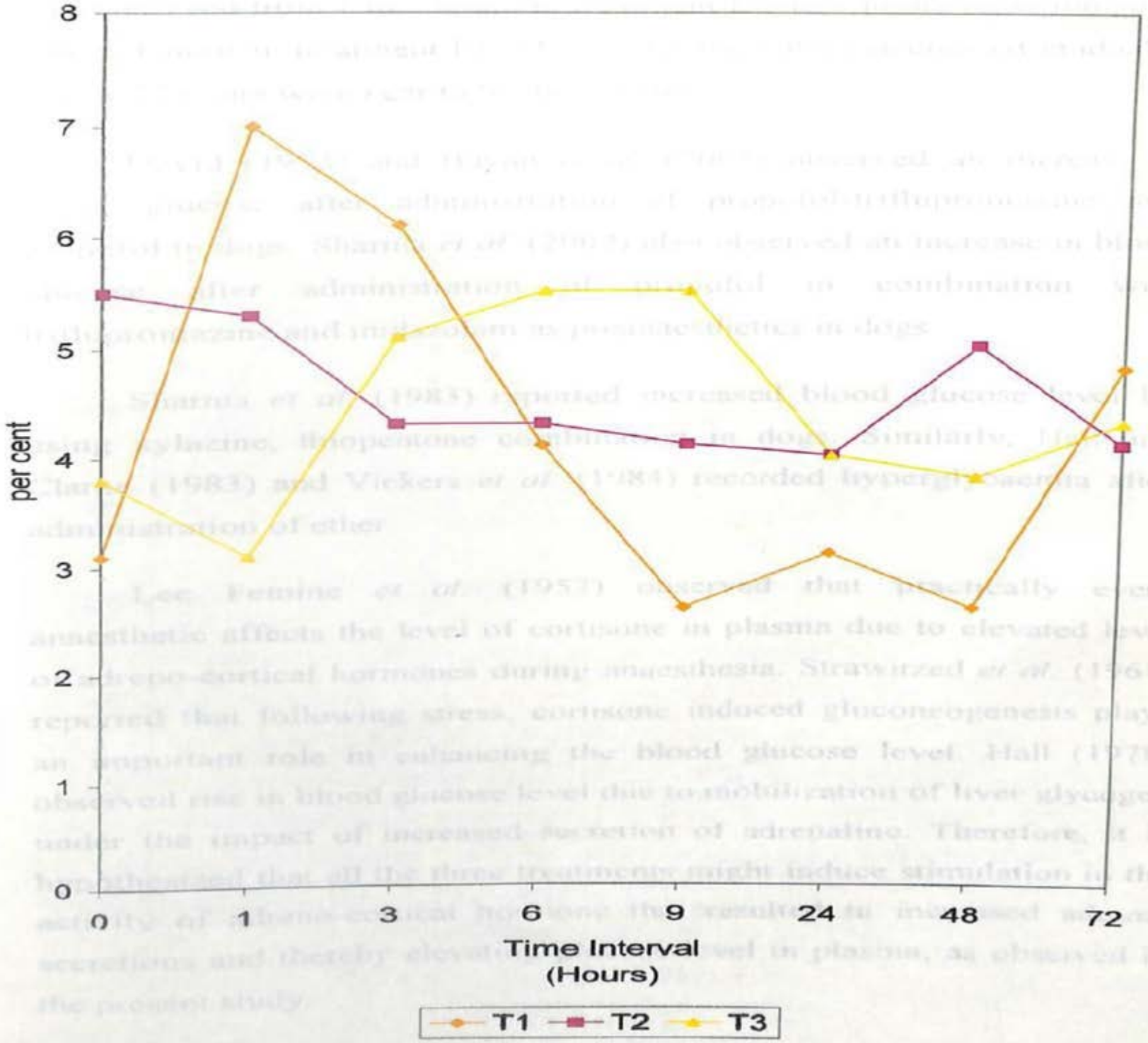


FIG. 14 : EOSINOPHIL COUNT AFTER ADMINISTRATION OF PROPOFOL AND ANAESTHETIC ETHER IN COMBINATION WITH PREANAESTHETICS IN DOGS



C. BIOCHEMICAL STUDIES

Plasma Glucose

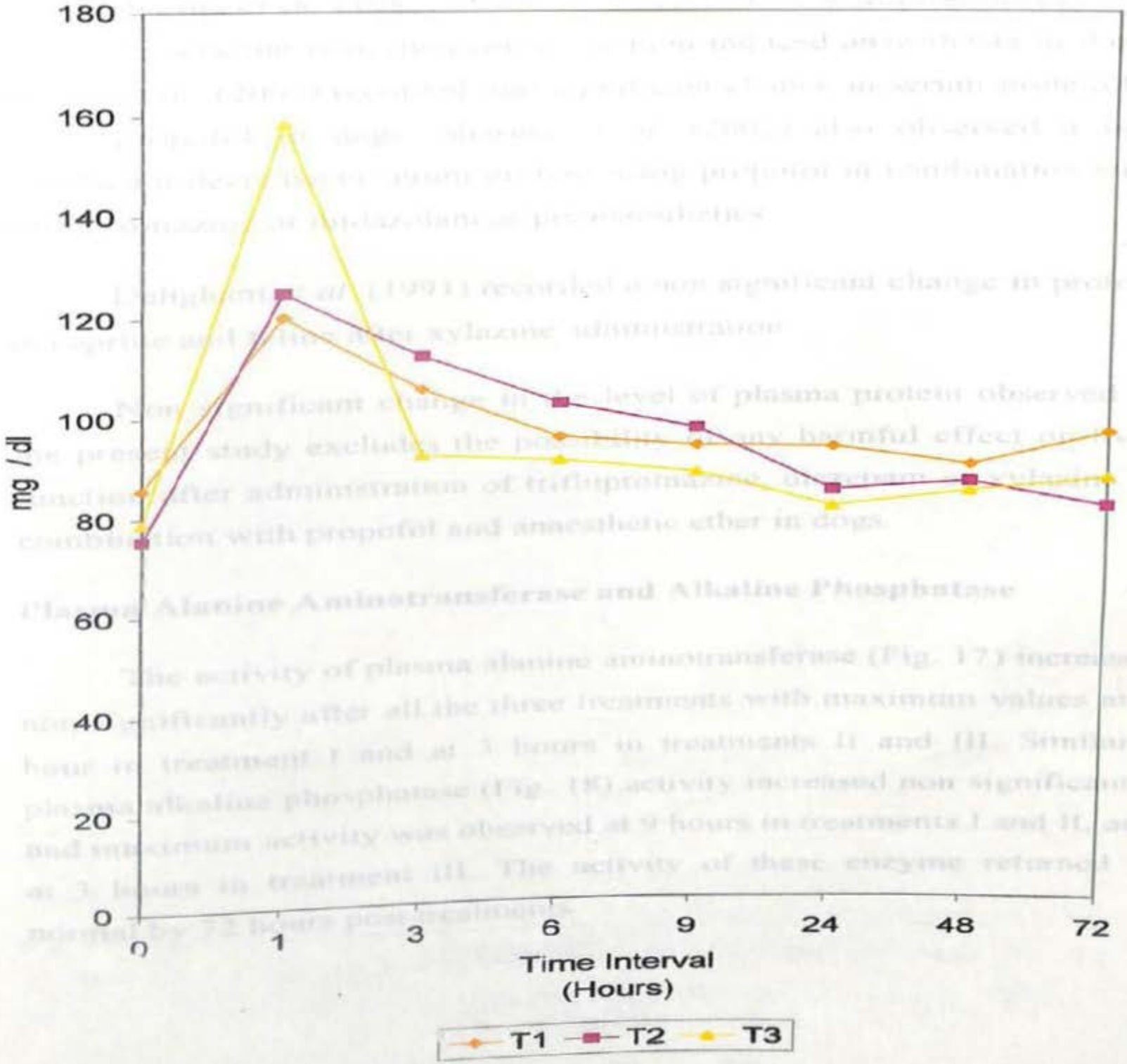
A significant increase in plasma glucose concentration (Fig. 15) was observed from 1 to 3 hours in treatment I, 1 to 6 hours in treatment II and at 1 hour in treatment III. There after the values decreased gradually and at 72 hours were near to '0' hour value.

David (1993) and Bayan *et al.* (2002) observed an increase in blood glucose after administration of propofol-triflupromazine and propofol in dogs. Sharma *et al.* (2002) also observed an increase in blood glucose after administration of propofol in combination with triflupromazine and midazolam as preanaesthetics in dogs.

Sharma *et al.* (1983) reported increased blood glucose level by using xylazine, thiopentone combination in dogs. Similarly, Hall and Clarke (1983) and Vickers *et al.* (1984) recorded hyperglycaemia after administration of ether.

Lee Femine *et al.* (1957) observed that practically every anaesthetic affects the level of cortisone in plasma due to elevated level of adreno-cortical hormones during anaesthesia. Strawitzed *et al.* (1961) reported that following stress, cortisone induced gluconeogenesis plays an important role in enhancing the blood glucose level. Hall (1978) observed rise in blood glucose level due to mobilization of liver glycogen under the impact of increased secretion of adrenaline. Therefore, it is hypothesized that all the three treatments might induce stimulation in the activity of adreno-cortical hormone that resulted in increased adrenal secretions and thereby elevating glucose level in plasma, as observed in the present study.

FIG. 15 : PLASMA GLUCOSE AFTER ADMINISTRATION OF PROPOFOL AND ANAESTHETIC ETHER IN COMBINATION WITH PREANAESTHETICS IN DOGS



Plasma Protein

A non significant change in the values of total protein was observed after all the three treatments.

Sharma *et al.* (1983) observed a decrease in total protein (Fig. 16) by using xylazine with thiopentone sodium induced anaesthesia in dogs. Bayan *et al.* (2002) recorded non significant change in serum protein by using propofol in dogs. Sharma *et al.* (2002) also observed a non significant decrease in serum protein using propofol in combination with triflupromazine or midazolam as preanaesthetics.

Dehghani *et al.* (1991) recorded a non significant change in protein in caprine and feline after xylazine administration.

Non significant change in the level of plasma protein observed in the present study excludes the possibility of any harmful effect on liver function after administration of triflupromazine, diazepam or xylazine in combination with propofol and anaesthetic ether in dogs.

Plasma Alanine Aminotransferase and Alkaline Phosphatase

The activity of plasma alanine aminotransferase (Fig. 17) increased non significantly after all the three treatments with maximum values at 1 hour in treatment I and at 3 hours in treatments II and III. Similarly plasma alkaline phosphatase (Fig. 18) activity increased non significantly and maximum activity was observed at 9 hours in treatments I and II, and at 3 hours in treatment III. The activity of these enzyme returned to normal by 72 hours post treatments.

FIG. 16 : PLASMA PROTEIN AFTER ADMINISTRATION OF PROPOFOL AND ANAESTHETIC ETHER IN COMBINATION WITH PREANAESTHETICS IN DOGS

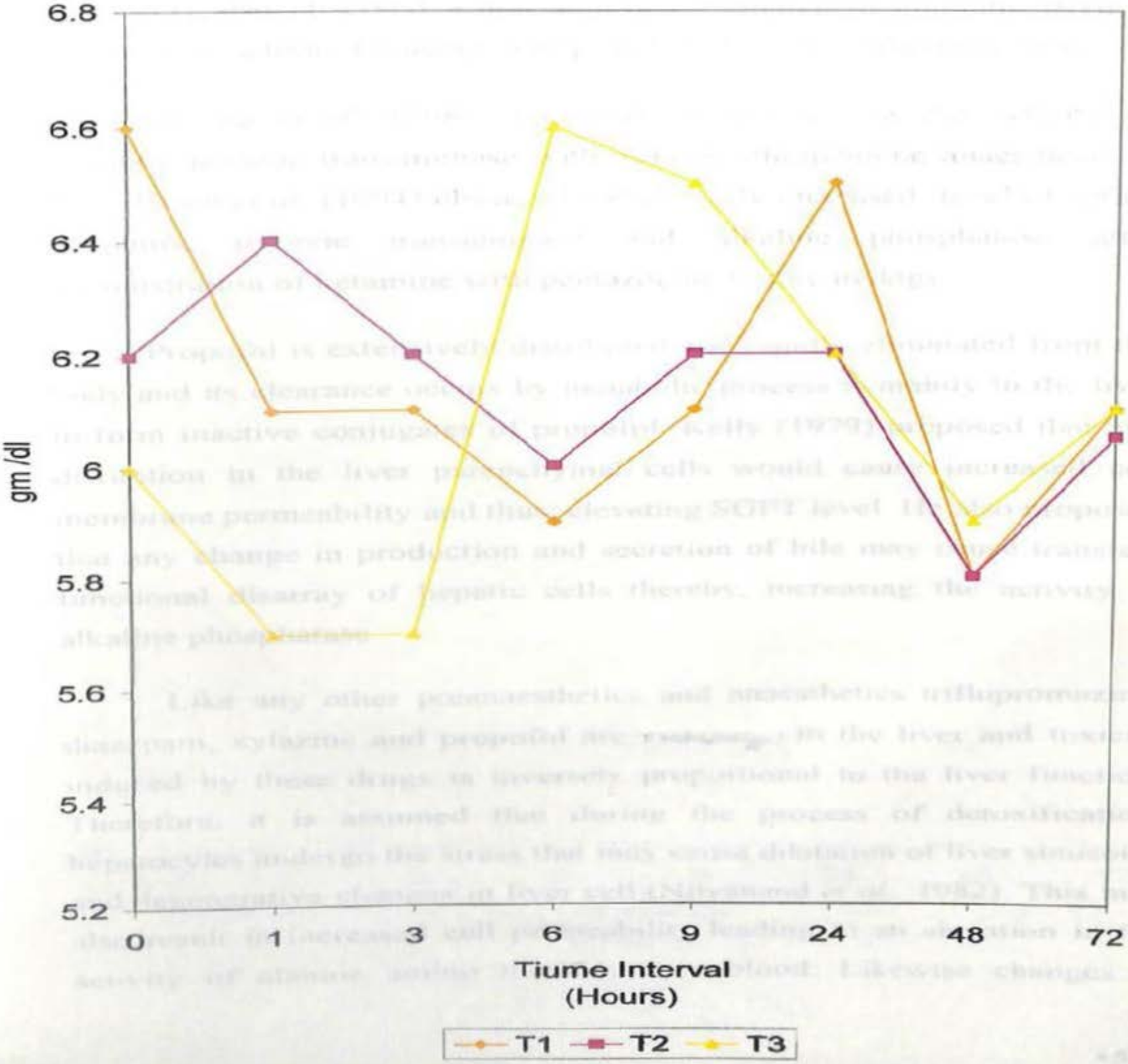
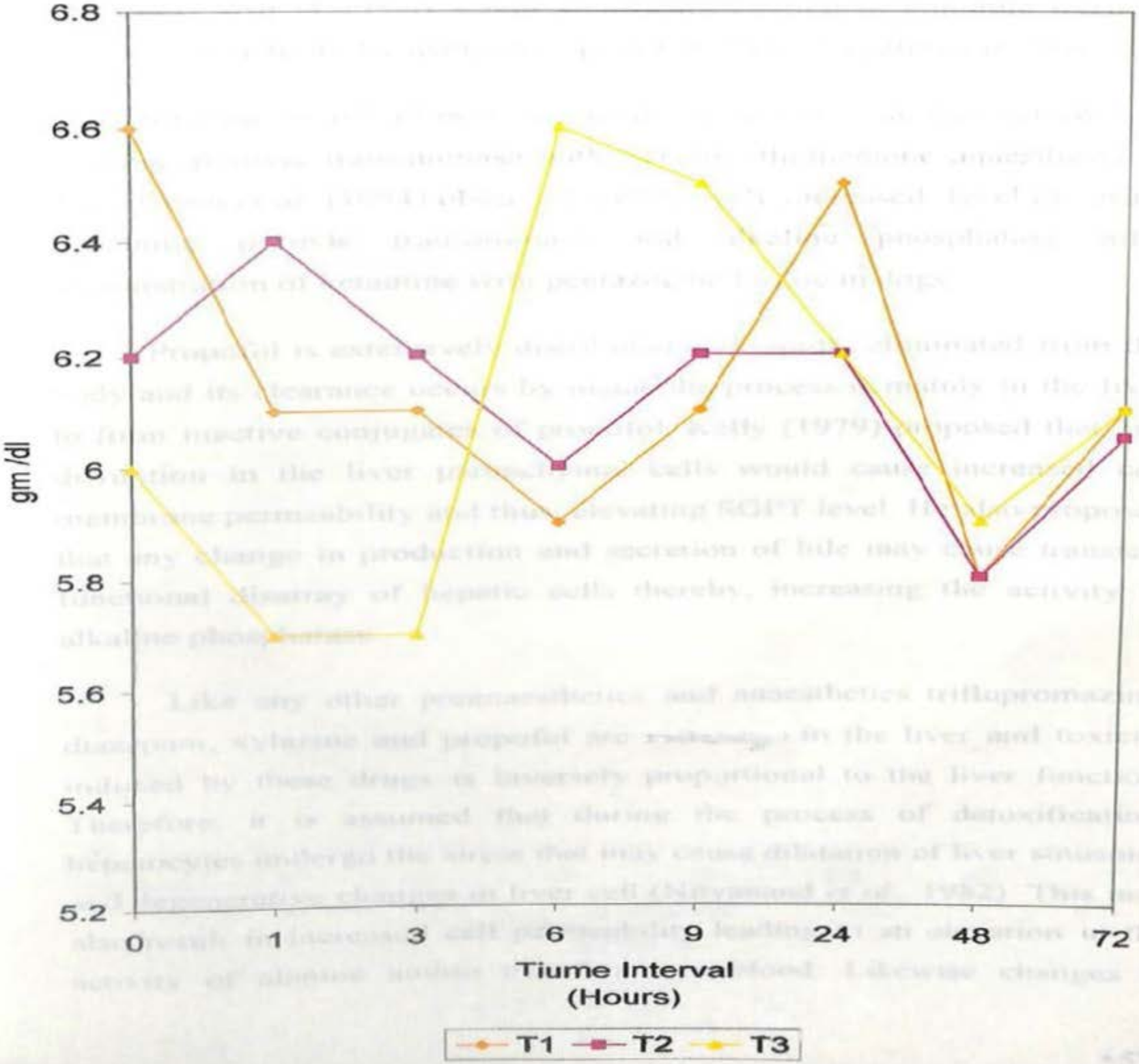


FIG. 16 : PLASMA PROTEIN AFTER ADMINISTRATION OF PROPOFOL AND ANAESTHETIC ETHER IN COMBINATION WITH PREANAESTHETICS IN DOGS



Sharma *et al.* (2002) observed non significant increase in alkaline phosphatase activity whereas the activity of glutamic pyruvic transaminase remained unaltered after administration of propofol along with triflupromazine and midazolam as preanaesthetics in dogs. Singh *et al.* (1999) also observed a non significant change in glutamic pyruvic transminase activity by using diazepam-ketamine anaesthesia in goats.

Sharma *et al.* (1983) recorded an increase in the activity of glutamic pyruvic transaminase with xylazine-thiopentone anaesthesia in dogs. Bisen *et al.* (1994) observed significantly increased level of serum glutaminc pyruvic transaminase and alkaline phosphatase after administration of ketamine with pentazocine lactate in dogs.

Propofol is extensively distributed and rapidly eliminated from the body and its clearance occurs by metabolic process is mainly in the liver to form inactive conjugates of propofol. Kelly (1979) proposed that any disruption in the liver parenchymal cells would cause increased cell membrane permeability and thus, elevating SGPT level. He also proposed that any change in production and secretion of bile may cause transient functional disarray of hepatic cells thereby, increasing the activity of alkaline phosphatase.

Like any other preanaesthetics and anaesthetics triflupromazine, diazepam, xylazine and propofol are metabolized in the liver and toxicity induced by these drugs is inversely proportional to the liver function. Therefore, it is assumed that during the process of detoxification, hepatocytes undergo the stress that may cause dilatation of liver sinusoids and degenerative changes in liver cell (Nityanand *et al.*, 1982). This may also result in increased cell permeability leading to an elevation in the activity of alanine amino transferase in blood. Likewise changes in

FIG. 17 : PLASMA ALANINE AMINO TRANSFERASE AFTER ADMINISTRATION OF PROPOFOL AND ANAESTHETIC ETHER IN COMBINATION WITH PREANAESTHETICS IN DOGS

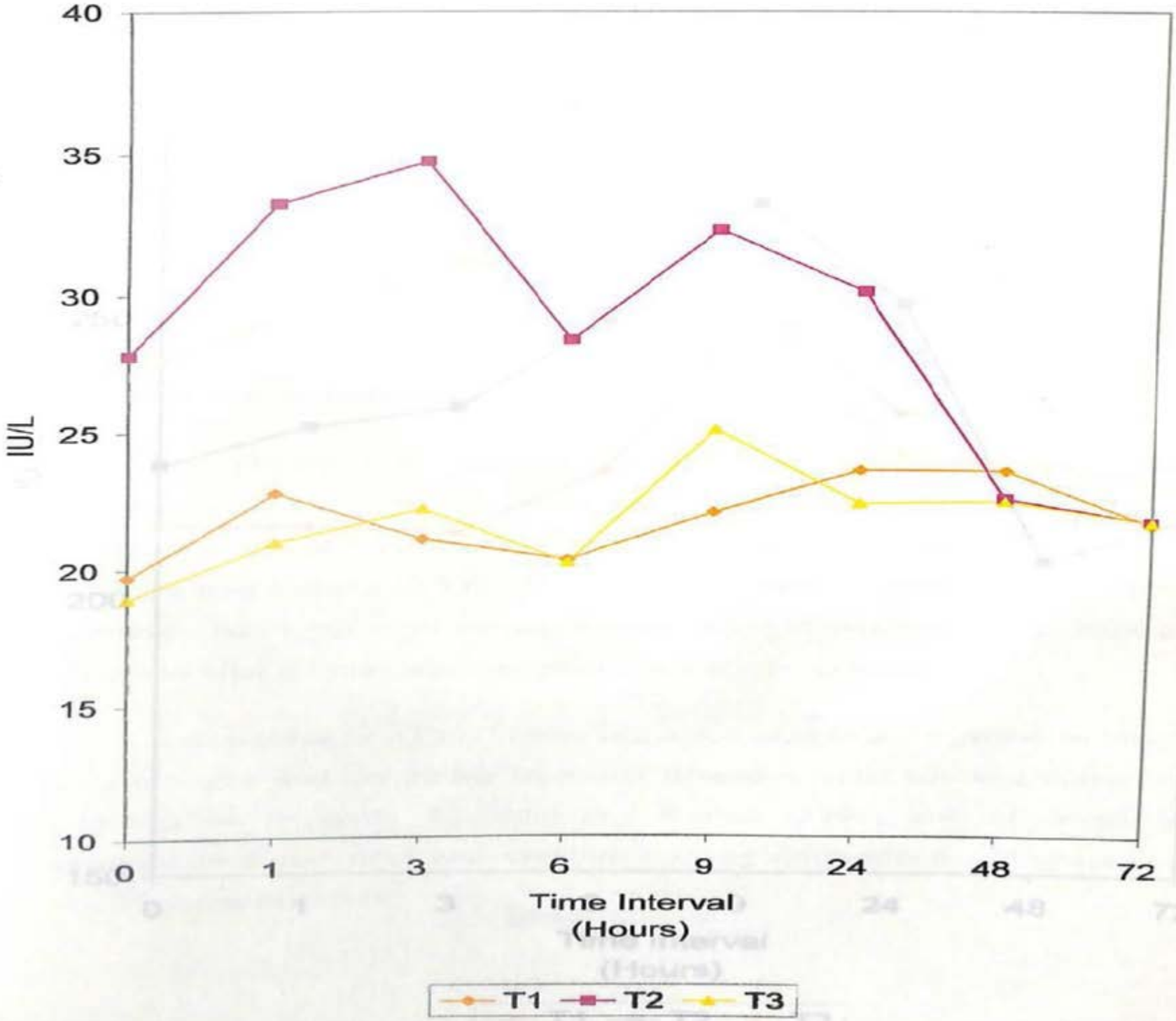
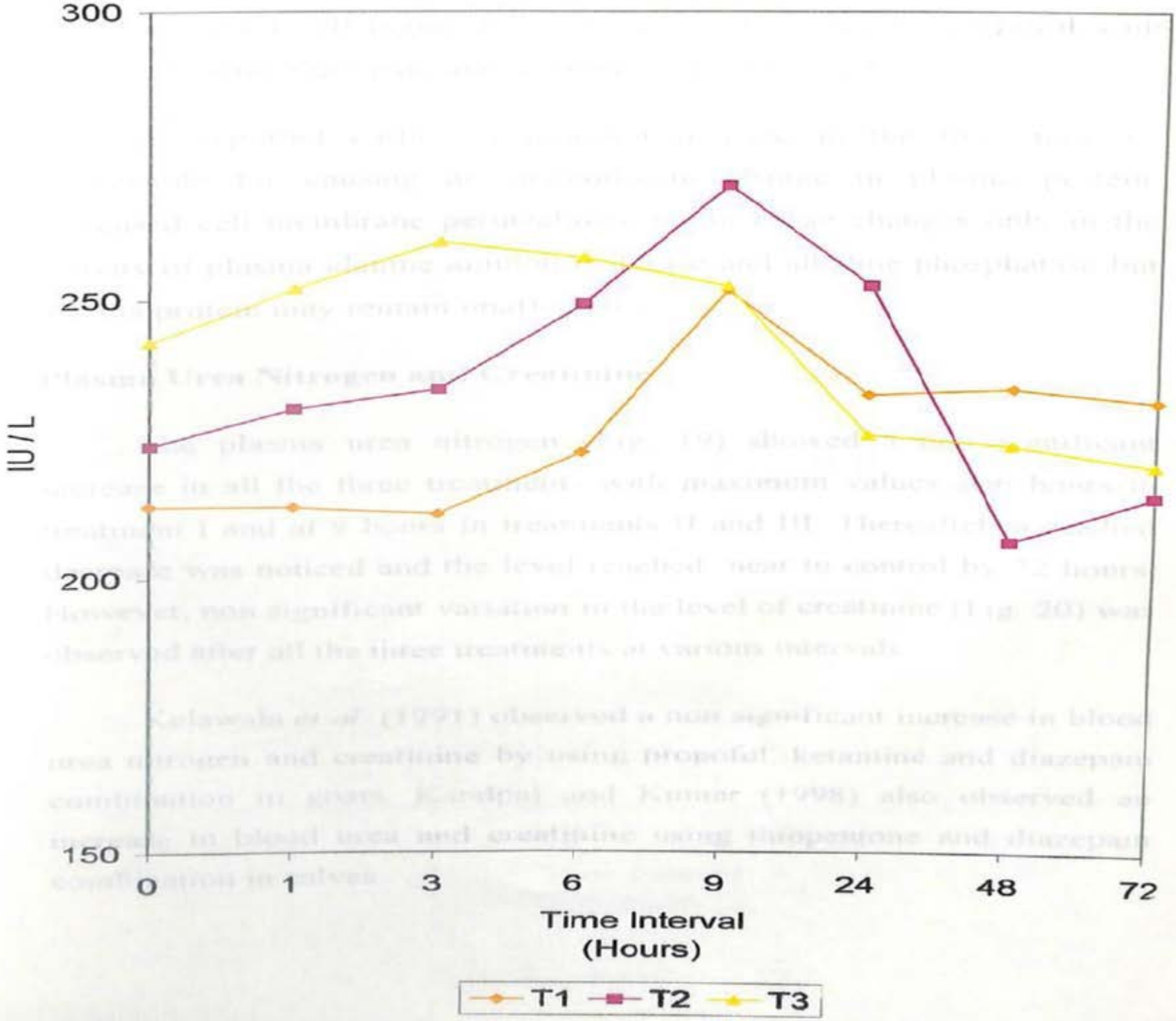


FIG. 18 : PLASMA ALKALINE PHOSPHATASE AFTER ADMINISTRATION OF PROPOFOL AND ANAESTHETIC ETHER IN COMBINATION WITH PREANAESTHETICS IN DOGS



production and secretion of bile will result in stimulating the activity of alkaline phosphatase (Kelly, 1979).

It may therefore be assumed that, the observed non significant increase in level of alanine amino transferase and alkaline phosphatase may be due to slight disruption of liver parenchymal cell as well as due to slight increased cell permeability by intravenous use of propofol with triflupromazine, diazepam and xylazine as preanaesthetics.

As reported earlier, a minimal damage in the liver may be responsible for causing an insignificant change in plasma protein. Increased cell membrane permeability might cause changes only in the activity of plasma alanine aminotransferase and alkaline phosphatase but plasma protein may remain unaffected.

Plasma Urea Nitrogen and Creatinine

The plasma urea nitrogen (Fig. 19) showed a non significant increase in all the three treatments with maximum values at 6 hours in treatment I and at 9 hours in treatments II and III. Thereafter, a gradual decrease was noticed and the level reached near to control by 72 hours. However, non significant variation in the level of creatinine (Fig. 20) was observed after all the three treatments at various intervals.

Kelawala *et al.* (1991) observed a non significant increase in blood urea nitrogen and creatinine by using propofol, ketamine and diazepam combination in goats. Kandpal and Kumar (1998) also observed an increase in blood urea and creatinine using thiopentone and diazepam combination in calves.

FIG. 19 : PLASMA UREA NITROGEN AFTER ADMINISTRATION OF PROPOFOL AND ANAESTHETIC ETHER IN COMBINATION WITH PREANAESTHETICS IN DOGS

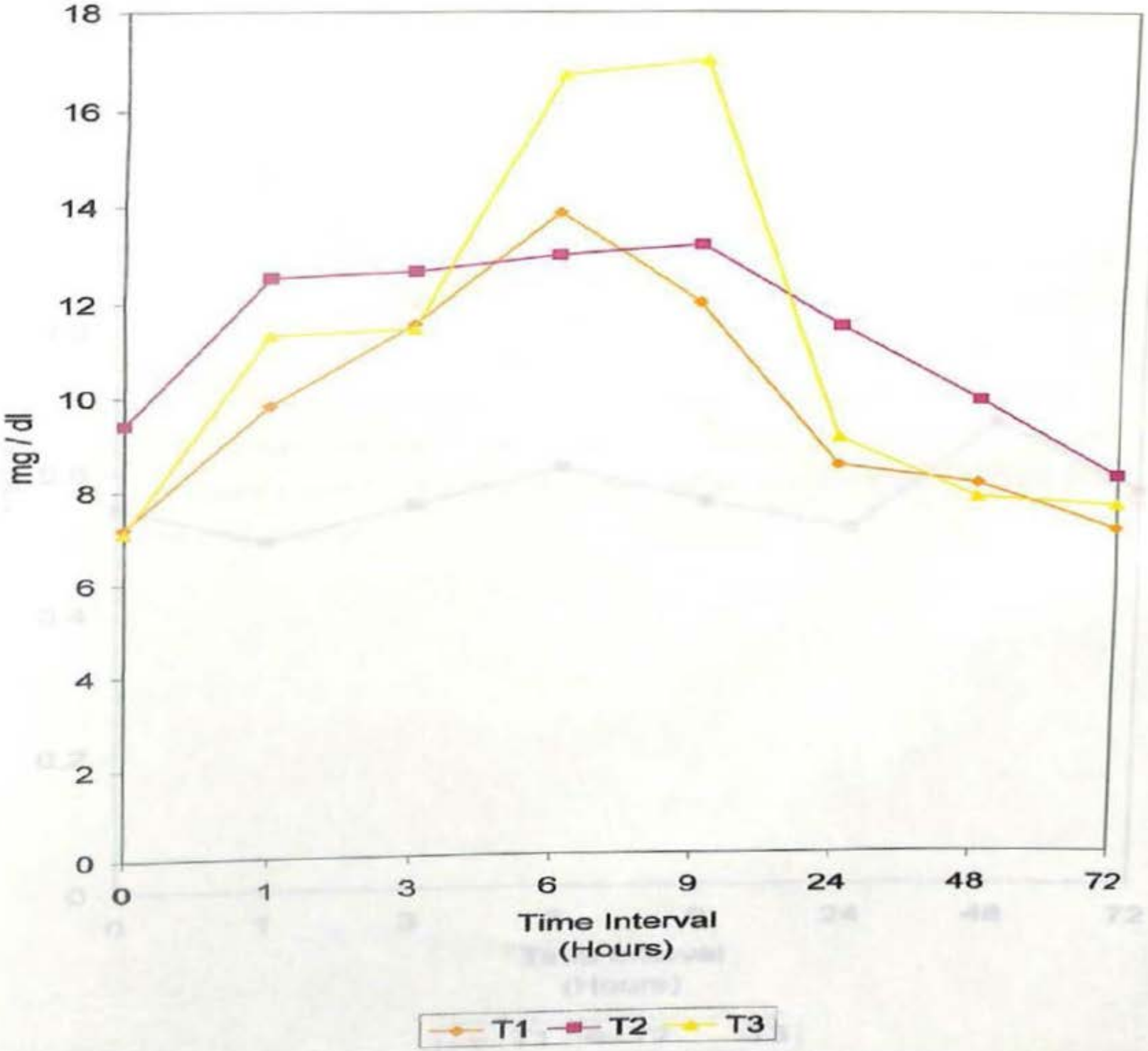
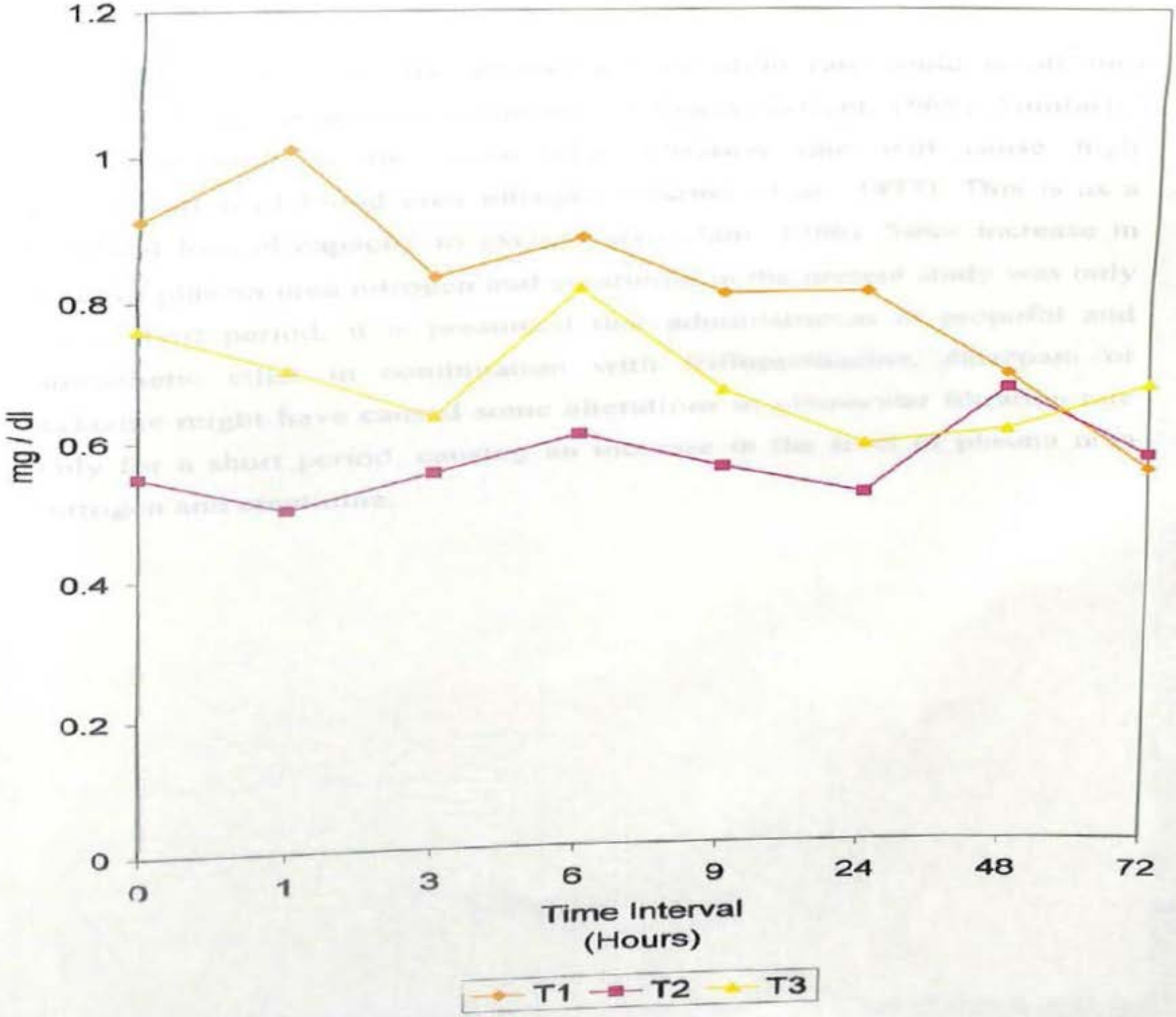


FIG. 20 : PLASMA CREATININE AFTER ADMINISTRATION OF PROPOFOL AND ANAESTHETIC ETHER IN COMBINATION WITH PREANAESTHETICS IN DOGS



Jiwan and In ho (1999) recorded increase in blood urea nitrogen after administration of propofol and xylazine in dogs. Similarly, Sharma (2002) also observed non significant increase in blood urea nitrogen and no significant change in creatinine by using triflupromazine, midazolam as preanaesthetics in combination with propofol as general anaesthetic in dogs.

The increase in the glomerular filtration rate could result into increased concentration of creatinine in blood (Wright, 1965). Similarly, any retardation in the glomerular filtration rate will cause high concentration of blood urea nitrogen (Garner *et al.*, 1977). This is as a result of loss of capacity to excrete urea (Jain, 1986). Since increase in level of plasma urea nitrogen and creatinine in the present study was only for a short period, it is presumed that administration of propofol and anaesthetic ether in combination with triflupromazine, diazepam or xylazine might have caused some alterations in glomerular filtration rate only for a short period, causing an increase in the level of plasma urea nitrogen and creatinine.

~~~ Summary

SUMMARY

Six apparently healthy mongrel adult dogs of either sex, weighing approximately 10-20 kg were used for the present experiment. The dogs were kept on a uniform diet and management during entire period of experiment.

To obtain baseline values before commencement of actual experiment, clinical parameters viz. rectal temperature, pulse and respiration rates were recorded. Three blood samples were also collected from each animal and analysed for various haematological attributes i.e. total erythrocyte and leucocyte count, differential leucocyte count, haemoglobin concentration and packed cell volume. The biochemical parameters analyzed were plasma glucose, total protein, alanine aminotransferase, alkaline phosphatase, urea nitrogen and creatinine.

Each dog was subjected to three different treatments and each treatment lasted for four days. A rest period of eight days was provided before the start of next treatment.

Atropine sulphate @ 0.05 mg/kg b.wt. was administered I.M. in all the three treatments. In treatment I, triflupromazine hydrochloride was administered @ 1 mg/kg b.wt. I.V. followed by propofol (1%) I.V., 10 minutes after the triflupromazine, till the loss of paedal reflex. The anaesthesia was maintained for half an hour with anaesthetic ether using semiclose method. In treatment II diazepam @ 2 mg/kg b.wt. I.V. was given 10 minutes after, followed by propofol and anaesthetic ether as in treatment I. In treatment III xylazine @ 1.5 mg/kg wt. I.M., after 10

minutes it was followed by propofol and anesthetic ether as in treatment I.

The rectal temperature, heart rate and respiration rates were recorded at 0, 10, 20, 30 minutes and at 1, 2, 3, 4, 5, 6, 9, 24 and 48 hours post treatment. The '0' hour value was recorded just before the start of treatment and was treated as control.

The blood samples were collected at 0 hour and subsequently at 1, 3, 6, 9, 24, 48 and 72 hours post treatment for various haematological and biochemical estimations.

The duration of surgical anesthesia was 38.33 ± 4.40, 34.16 ± 1.35 and 46.83 ± 5.32 minutes, whereas complete recovery from anaesthesia was in 60.83 ± 18.40, 68.33 ± 22.45 and 43.33 ± 9.54 minutes in treatments I, II and III respectively. The dose of propofol used to induce surgical anesthesia was 4.28 ± 0.47, 4.41 ± 0.40 and 2.82 ± 0.06 mg/kg b.wt., while the amount of ether used to maintain the anaesthesia for half an hour after the induction with propofol was 3.53 ± 0.95, 3.54 ± 0.60 and 3.60 ± 0.42 ml/kg b.wt. in treatments I, II and III respectively.

The rectal temperature decreased non significantly with the minimum values at 1 hour in treatments I and II and at 2 hours in treatment III. Respiration rate showed significant increase ($P<0.05$) at 30 minutes in treatments I and II, whereas in treatment III significant decrease ($P<0.05$) was observed from 1 to 3 hours. Heart rate showed significant increase ($P<0.05$) from 10 minutes to 1 hour in treatments I and II and between 10 to 30 minutes in treatment III.

Total erythrocyte count showed a non significant decreasing trend with minimum values at 1 hour in treatment I and at 3 hours in treatments II and III. Packed cell volume showed non significant decrease with minimum values at 3 hours in treatments I and III, while at 6 hours in treatment II. Similarly haemoglobin concentration also showed a non significant decreasing trend with minimum values at 9, 6 and 1 hour in treatments I, II, III respectively. A non significant change in total leucocyte count was observed in all the three treatments. Significant increase ($P<0.05$) in neutrophil count was noticed from 1 to 9 hours in all the three treatments, where as lymphocyte count showed significant decrease ($P<0.05$) at 6 hours in treatments I and II while at 3 hours in treatment III. The monocyte count increased significantly ($P<0.05$) and the maximum values were observed at 3 hours in treatment I and at 6 hours in treatments II and III. A non significant difference was recorded in eosihophil count in all the three treatments. Basophil were observed occasionally in all the three treatments.

Plasma glucose concentration showed significant increase ($P<0.05$) from 1 to 3 hours in treatment I, at 1 to 6 hours in treatments II and at 1 hour in treatment III. A non significant variation in the level of total protein was observed in all the three treatments. The activity of alanine amino transeferase increased non-significantly with maximum level at 1 hour in treatment I and at 3 hours in treatments II and III. Activity of plasma alkaline phosphatase increased non-significantly and maximum values were observed at 9 hours in treatments I and II, where as at 3 hours in treatment III. Plasma urea nitrogen showed non significant increase with maximum values at 6 hours in treatment I, and at 9 hours in treatments II and III, while creatinine did not reveal any significant variation in all the three treatments.

CONCLUSION

On the basis of the results obtained in the present study, it is concluded that :

1. Propofol @ 2.82 to 4.41 mg/kg b.wt. to induce the general anesthesia and to maintain with anaesthetic ether @ 3.53 to 3.60 ml/kg b.wt. to prolong general anaesthesia for half an hour, is safe and economical.
2. Propofol and anaesthetic ether in combination with triflupromazine @ mg/kg b.wt., diazepam @ 2mg/kg b.wt. or xylazine @ 1.5 mg/kg b.wt. as preanaesthetics produces a quite and rapid onset of anaesthesia with smooth and faster recovery.
3. Propofol and anaesthetic ether in combination with preanaesthetics do not have any cumulative side effects as is indicated by faster recovery.
4. To produce the anaesthesia of longer duration with faster recovery and minimum dose of propofol and ether, xylazine as preanaesthetic is better followed by triflupromazine and diazepam.
5. The clinical, haematological and biochemical changes induced by propofol and ether along with triflupromazine, diazepam or xylazine as preanaesthetics, were of transient in nature and suggestive of least temporary alterations in cardio-respiratory, liver and kidney functions.

Thus, it can be concluded that anaesthetic ether can be safely used to prolong the anaesthesia induced by propofol in combination with triflupromazine, diazepam or xylazine. These combinations can be used conveniently without any complications for the surgical interventions of shorter or longer duration in canines.

Suggestions for Further Work

SUGESSIONS FOR FURTHER WORK

1. The systemic toxicity of propofol and anaesthetic ether with triflupromazine, diazepam or xylazine may be assessed by undertaking histopathological studies of liver, kidney, cerebrum, hypothalamus, myocardium and bone marrow in laboratory animals.

2. The study may be planned to observe the changes in the body fluids and electrolytes following triflupromazine, diazepam or xylazine with propofol and anaesthetic ether.

3. The study may be planned to observe the effects of these combinations on clinical cases.

4. The experimental studies may be carried out by electroencephalography and electrocardiography for better understanding the effects on cardiac and neurological functions with these combinations.

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VITA

The author, Dr. Reshma Jain was born on 10th July 1976 at Patan. She passed her Higher Secondary School Certificate Examination from Govt. M.L.B. School, Jabalpur with First Division in the year 1993. She obtained degree of Bachelor of Veterinary Science and Animal Husbandry from College of Veterinary Science and Animal Husbandry, J.N.K.V.V., Jabalpur (M.P.) with 7.12 O.G.P.A. out of 10 point scale in the year 2000.

In September, 2001 She joined her M.V.Sc. & A.H. programme in the Department of Veterinary Surgery and Radiology, College of Veterinary Science & A.H., J.N.K.V.V., Jabalpur.

She has worked under a project as Junior Research Fellow from June 2001 to Aug. 2001, in the Department of Animal Breeding & Genetics, College of Veterinary Science and A.H., J.N.K.V.V., Jabalpur. She is a life member of Indian Society for Veterinary Surgery.

Permanent Address: ~
C/o Dr. Rajkumar Jain
244, Indrapuri
Bhanwarkua, Indore.

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