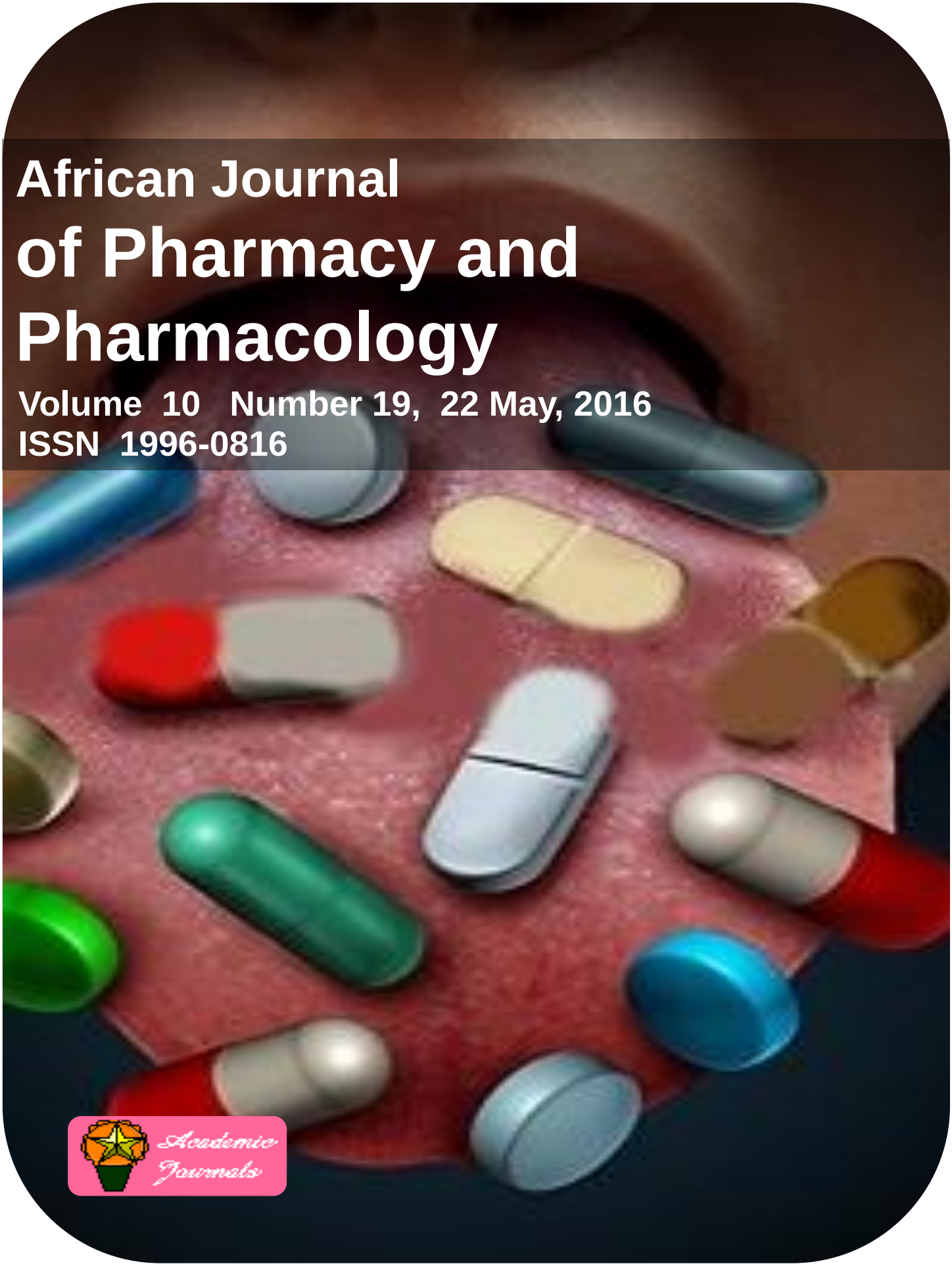

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Full Length Research Paper

Evaluation of Hepatic activity of various morphological parts of *Musa paradisiaca* L.

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The objective of present study was to investigate the hepatic activity of methanolic extract of various morphological parts (bract, flower, trachea and tracheal fluid) of *Musa paradisiaca* L. for their effect on liver of experimental mice. The methanolic extract of morphological parts of *Musa paradisiaca* (bract, flower, trachea and tracheal fluid) at the dose of (100, 250 and 500 mg/kg b.w) and silymarin (25 mg/kg) was orally administered once daily for 28 days and toxicity evaluation studies were carried out. Liver damage was assessed by biochemical parameters such as total bilirubin, direct bilirubin, indirect bilirubin, alkaline phosphatase (ALP), alanine transaminase (ALT), aspartate aminotransferase (AST), serum protein, serum albumin, serum globulin and A/G ratio and by histopathology of carbon tetrachloride (CCl_4) induced hepatic injury in mice. Results of the experiment showed that there is significant ($P< 0.05$) diversity between the groups that were treated with CCl_4, silymarin and different doses of different morphological parts of plant as compared to control group. Histopathological studies also supported the biochemical parameters. Different morphological parts of *M. paradisiaca* such as bracts, flower, trachea and tracheal fluid have potential to cause the hepatotoxicity that depends on the dose and the time duration in experimental mice.

Key words: *Musa paradisiaca* L., hepatic activity, histopathology, biochemical parameters.

INTRODUCTION

The liver, a major body organ plays an important role in the metabolism of the lipids, protein and carbohydrates, metabolic homeostasis, detoxification, biotransformation and excretion of many endogenous, environmental and pharmaceutical chemicals storage of glycogen, biochemical's necessary for digestion (bile), production of several coagulation factors, hormones (angiotensinogen), growth factors, vitamin A, D and B12 and protects the body from toxic by-products of metabolisms and potentially injurious substances namely endotoxins that are absorbed from the intestinal tract (Zhang et al., 2014; Madhu et al., 2012; Ajith et al., 2007). In last few decades liver injury and dysfunction is mainly caused due to exposure to toxic chemicals, certain drugs such as

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chemotherapeutic agents, thio-acetamide, carbon tetrachloride, xenobiotics, chronic alcohol consumption, microbes, environmental pollutants, viruses, and auto-immune diseases (Zhang et al., 2014; Showkat et al.,2013; Mohanraj et al., 2013).

Carbon tetrachloride is a potent hepatotoxin that metabolized to tri-chloromethyl radicals by cytochrome P_{450} which leads to increase in hepatic lipid peroxidation and oxidative stress that why widely used to produce hepatotoxicity to evaluate hepatoprotective effects of natural products (Ottu et al., 2013). There are many reports which show similarities between CCl_4 induced liver damage and human liver cirrhosis (Halim et al., 1997). That is why CCl_4 induced liver damage is generally used as experimental model for screening of hepatoprotective and hepatocurative drugs.

The intensity of hepatic damage is generally accessed by measuring the activities of hepatic cytoplasmic enzymes [serum glutamate pyruvate transaminase (SGPT), serum glutamate oxalacetate transaminase (SGOT), serum alkaline phosphatase (ALP)], serum bilirubin concentration and histological studies (Stierum, 2005). The extent of oxidative stress may be predicted by estimating the serum glutathione level (Sallie et al., 1991).

In recent years natural products and their active principles are the sources for new drug discovery and treatment of diseases (Ajith et al., 2007). Lack of toxicity and claims of therapeutic efficiency of many plants in recent years have been proved scientifically. In view of the potential use of medicinal plants as a source of alternative medicine in many diseases and claims made by the people in different countries, many species of plants kingdom containing chemical constituent of medicinal value which have to be discovered yet. Large numbers of plants are needs to be examined thoroughly for their possible pharmacological value (Ethadi et al., 2013; Tauqeer et al., 2014).

Musa paradisiaca L. (Musaceae) is evergreen tropical monoherbacious plant,commonly known as kela (Urdu) Kadali, Bali Hannu (Hindi) and Plantain (English). It is major food crops in the humid and subhumid parts of Pakistan, Africa, India, Burma, Bangladesh, America, and Australia (Paul et al., 2013; Sanjeev et al., 2012; Sunil et al., 2012; Shodehinde et al., 2012). *M. paradisiaca* root is used as tonic for congestion of the liver and to prevent scurvy, anaemia, veneral disease.

The leaves are used in inflammation of eye, healing wounds and ulcers. The flowers check excessive bleeding during menstruation and are used in the case of diabetes. The fruits are used in diarrhea, indigestion and flatulence. The stems are used for ulcer, jaundice, nervous disorder, hysteria, diarrhea, dysentery, antidote for opium poisoning, asthma, hair loss, treatment of piles (Sanjeev et al., 2012; Enye et al., 2013).

Objective of our study was to evaluate the various morphological parts (bract, flower, trachea and tracheal fluid) of *M. paradisiaca* for its effect on liver.

MATERIALS AND METHODS

Plant material

M. paradisiac plant was collected from District Muzaffar-Garh, (Punjab) Pakistan during November 2013 and authenticated by Dr. Mansoor Hameed, Associate Professor, Taxonomic Laboratory, Department of Botany, University of Agriculture Faisalabad with voucher number 131-2014. Each part of plant was also deposited in the herbal museum Department of Pharmacognosy, Faculty of Pharmacy, University of Karachi. The parts of plant [bracts, flower and Flowering stalk (trachea)] were separated and dried in shade at room temperature for about one month.

Preparation of extract

2.5 kg bracts, 2.0 kg flowers and 2.0 kg trachea (flowering stalk) were coarsely powdered by mortar and pestle separately and then passed through sieve number 40 and stored in air tight container. Extraction was carried out separately for each part in 7.5, 5.0 and 4.0 L methanol (Merck, Germany) respectively in glass aspirator by maceration for seven days with occasional shaking at room temperature then filtration was carried out by using Whatman filter No 1. The filtrate were evaporated to dryness in rotary vacuum evaporator (Rotavapor R-200, Buchi) at temperature 45°C with rotation 3.0 rpm and pressure 0.07 MPA or 20 in Hg. The dried material were weighed, labeled and stored in refrigerator. 1.0 L tracheal fluid obtained from floral stalk after cutting the bunch of fruit and this is then, lyophilized at -65 to -60°C with vacuum of 30 to 40 milibar in alpha 1-4LSC Christ Germany lyophilizer. The dried material were weighed, labeled and stored in refrigerator (Sanyo biomedical freezer, MDF-U333, Japan).

Drugs and standards

Standard drug silymarin was obtained from A and K Pharmaceuticals. Carbon tetrachloride was purchased from Riedel De Haen. Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), total bilirubin, direct bilirubin, Alkaline phosphatase (ALP), Total protein, Albumin and Globulin reagents for estimation were purchased from Roche Pakistan Ltd. Animal feed pellets were purchased from local market. All other chemicals and solvents used in the study were of analytical grade (Merck, Germany).

Animal

Wistar mice of either sex weighing between 22 and 30 g were taken for the study. Animals were housed in colony cages under standardized conditions at a temperature of 24±2°C, humidity of 50% under 12 h light / dark cycle and they were fed with *ad libitum* with standard pellet diet with free access to food and water. They were allowed to acclimatize for a week before the experiments were started and protocol was approved by the Institutional animal ethics committee for the purpose of control and supervision on animals. The experimental procedures were carried out in strict compliance with the Institutional Animal Ethics committee (Ref. No. Pharm/14/1928).

Carbon tetrachloride-induced hepatotoxicity in mice

Effect of various morphological part of *M. paradisiaca* was tested using CCl_4 model as described by Kavishankara et al. (2014) with slight modification. The animals were randomly divided into fifteen

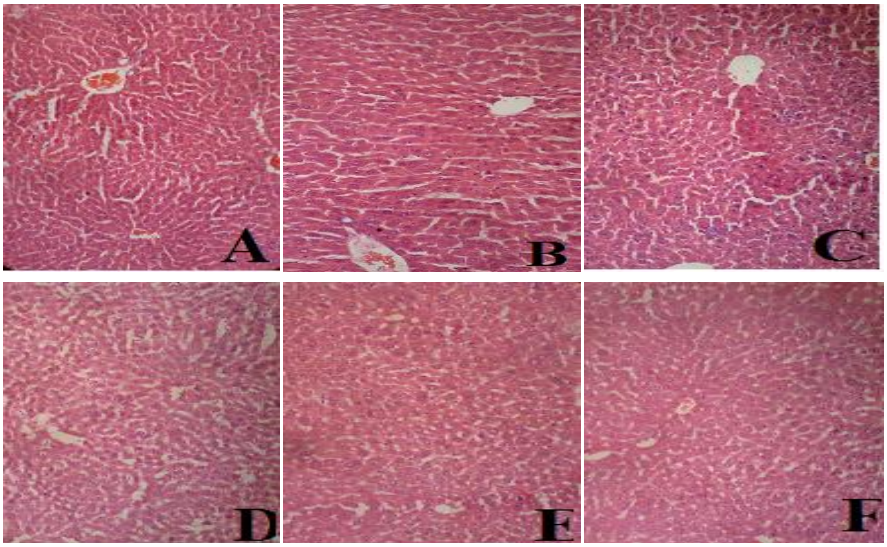

Figure 1. Photomicrographs showing the effect of silymarin, CCL_4, control group and different doses of bract extract of *M. paradisiaca* on mice liver. **A**: liver section of standard drug silymarin (25 mg/kg) treated group; **B:** liver section of CCL_4 (2.0 g/kg) treated group;**C**: normal control group receiving normal saline (2 ml/kg); **D**: methanolic extract of bract (100 mg/kg) treated group,**E**: methanolic extract of bract (250 mg/kg) treated group **F**: methanolic extract of bract (500 mg/kg) treated group (magnification ×10).

groups, consisting of six animals each. Group-I (negative control) received normal saline solution orally (0.2 ml/100 g); Group-II (toxic group) was given a single intraperitoneal dose of CCl_4 (2.0 g/kg b.w); Group-III (standard group) received orally 25 mg/kg b.w of silymarin; Group IV to VI (test groups), received a dose of (100, 250 and 500 mg/kg b.w., p.o.) of methanolic extract of bract of *M. paradisiaca* and CCl_4 (2.0 g/kg b.w., i.p.), respectively; Group VII to IX (test groups), received a dose of 100, 250 and 500 mg/kg b.w., p.o. of methanolic extract of flower of *M. paradisiaca* and CCl_4 (2.0 g/kg b.w., i.p.), respectively; Group X to XII (test groups), received a dose of 100, 250 and 500 mg/kg b.w., p.o. of methanolic extract of trachea of *M. paradisiaca* and CCl_4 (2.0 g/kg b.w., i.p.), respectively; Group XII to XV (test groups), received a dose of 100, 250 and 500 mg/kg b.w., p.o. of methanolic extract of tracheal fluid of *M. paradisiaca* and CCl_4 (2.0 g/kg b.w., i.p.), respectively. All the groups were treated for consecutive 28 days. On completion of experimental period, animals were sacrificed under ether anesthesia. Blood samples were collected and centrifuge. The obtained serums were analyzed for liver function markers. The liver was excised from the animal and immediately processed for histopathological studies (Kavishankara et al., 2014).

Histopathological studies

Mice were sacrificed, livers excised and tissues were washed in normal saline and fixed in10% formalin solution, dehydrated in graded (50 to 100%) alcohol and embedded in paraffin. 5 µm thin microtome sections were made, processed with alcohol-xylene series and stained with haematoxylin. It was then studied under light microscope for any histological protection or damage (Luna, 1968).

Biochemical measurement

Biochemical parameter like ALP, SGOT and SGPT, total bilirubin, direct bilirubin, total protein, albumin and globulin were determined by using automatic chemistry analyzer machine Cobas c311 by Roche.

Statistical analysis

The experimental data are expressed as mean ± SD. Data were subjected to statistical analysis through one way analysis of variance (ANOVA) followed by Tukey's test. The values of $P< 0.05$ is been considered as significant.

RESULTS

Histopathology

In histopathological study of CCl_4 induced hepatotoxicity model liver section of normal liver showed all cells with cellular organelles are normal; CCl_4 intoxicated group rat liver section showed degenerative changes in hepatocyte with vacuolation of cytoplasm and swelling of nucleus at some areas. Nuclear pyknosis was also observed. Cytoplasmolysis and necrotic changes were also present in hepatocytes that are the indication of cell damage; Sylimarin treated group rat liver section showed normal integrity of nucleus and cells.

The extract of bract of *M. paradisiaca* with different doses (100, 250 and 500 mg/kg) showed the moderate degenerative changes and dispersion of cytoplasm. Hepatic cords were shrinked. Necrotic changes in hepatocytes with pyknosis of nucleus at some places, vacuolization in cytoplasm and milder degrees of fatty changes (Figures 1 and 2). Flower extract at different

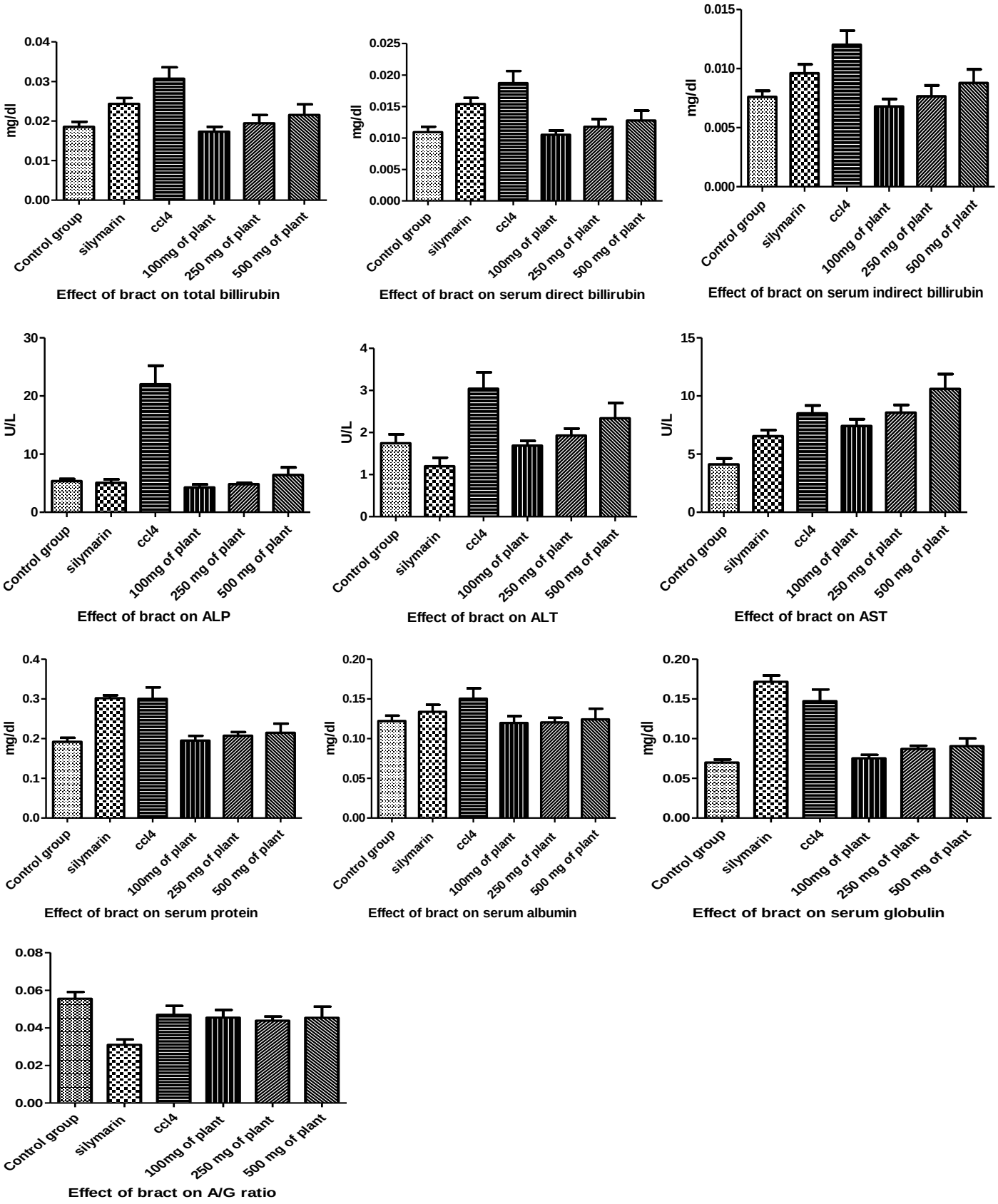

Figure 2. Effect of bract of *Musa paradisiaca* on liver parameters **(**total bilirubin, direct bilirubin, indirect bilirubin, ALP, ALT, AST, serum protein, serum albumin, serum globulin and A/G ratio).

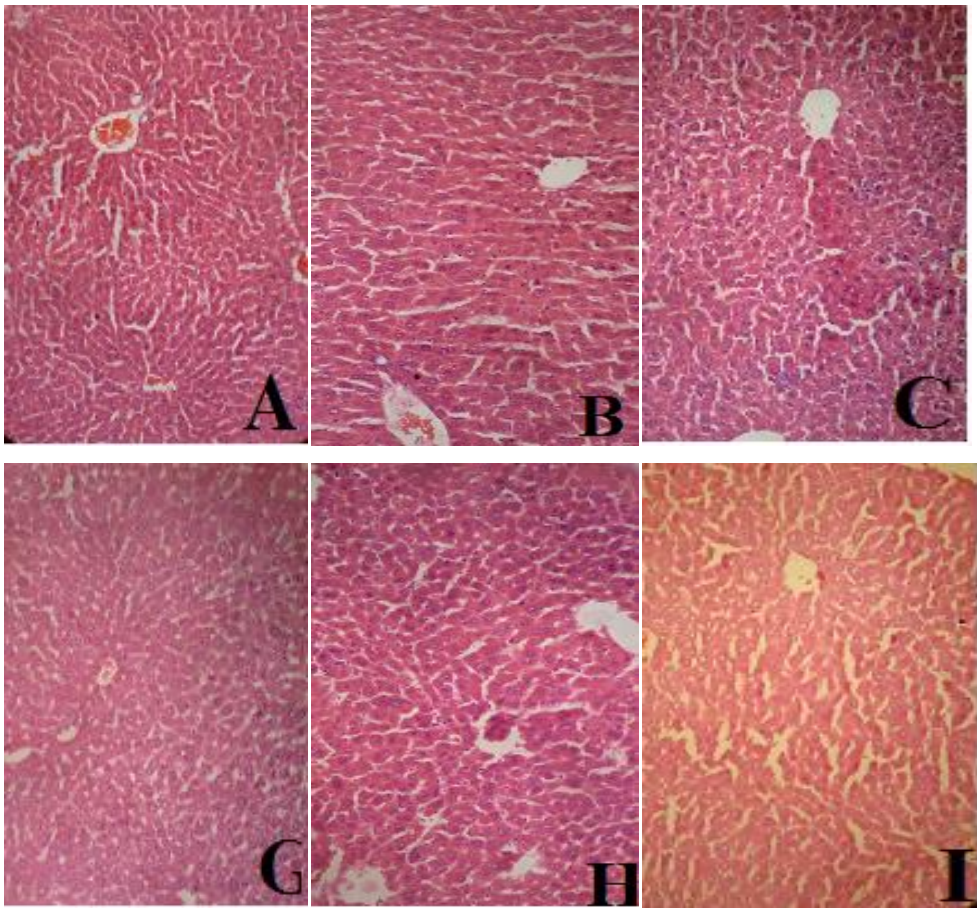

Figure 3. Photomicrographs showing the effect of silymarin, CCL_4, control group and different doses of flower extract of *M. paradisiaca* on mice liver. **A**: liver section of standard drug silymarin (25 mg/kg) treated group; **B**: liver section of CCL_4 (2.0 g/kg) treated group **C**: normal control group receiving normal saline (2 ml/kg); **G**: methanolic extract of flower (100 mg/kg) treated group **H**: methanolic extract of flower (250 mg/kg) treated group **I**: methanolic extract of flower (500 mg/kg) treated group (magnification ×10).

doses (100, 250, 500 mg/kg) shows that necrotic and degenerative changes were observed in group of cells with swollen nucleus at some places while pyknotic nucleus with more a sinophilic cytoplasm (Figure 3). *M. paradisiaca* tracheal extract at different doses (100, 250, and 500 mg/kg) shows slight dilation of sinusoidal spaces in liver cells and mild degree of fatty changes and vacuolization in cytoplasm of hepatocytes (Figure 4). While tracheal fluid of *M. paradisiaca* showed severe vacuolization, degenerative changes and a sinophilic cytoplasm with hyper-chromatic nucleus that has larger size (Figure 5 and 6).

Effect of extracts of *M. paradisiaca* on liver marker

In CCl_4 induced hepatotoxicity animal model pretreatment with silymarin (25 mg/kg) and methanolic extract of bract and trachea of *M. paradisiaca* at the dose of 100, 250 and 500 mg/kg reduced total bilirubin, direct bilirubin, indirect bilirubin, ALP, ALT, AST, serum protein, serum albumin, serum globulin and A/G ratio significantly ($P<0.05$), as compared with CCl_4 intoxicated (Figures 7). Less pronounced effect on liver marker was obtained from the flower and tracheal fluid extract of plant (Figures 4 and 8).

DISCUSSION

Hepatoprotective studies are conducted to investigate the protective effects of the plant extracts against liver damage. Major organ of the body is liver that can be injured by many drugs and chemicals (Hogade et al., 2010; Peng et al., 2009).

The hepatoprotective effects of methanolic extracts of *M. paradisiaca* (bract, flower, trachea and tracheal fluid) were studied in rats by using CCl_4 induced hepatotoxicity at the doses of 100, 250 and 500 mg/kg bw. Liver damage was assessed by biochemical studies

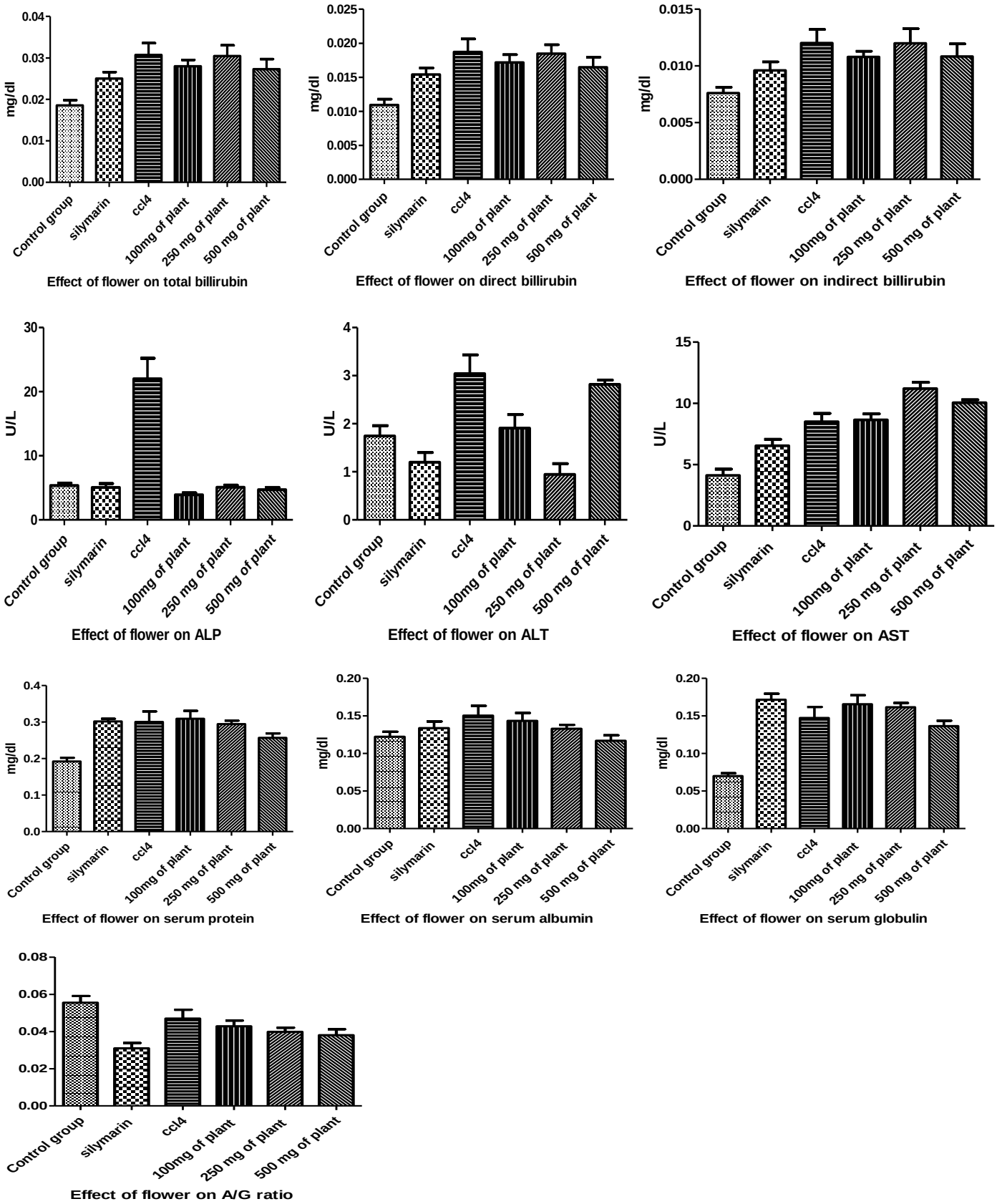

Figure 4. Effect of flower of *Musa paradisiaca* on liver parameters **(**total bilirubin, direct bilirubin, indirect bilirubin, ALP, ALT, AST, serum protein, serum albumin, serum globulin and A/G ratio).

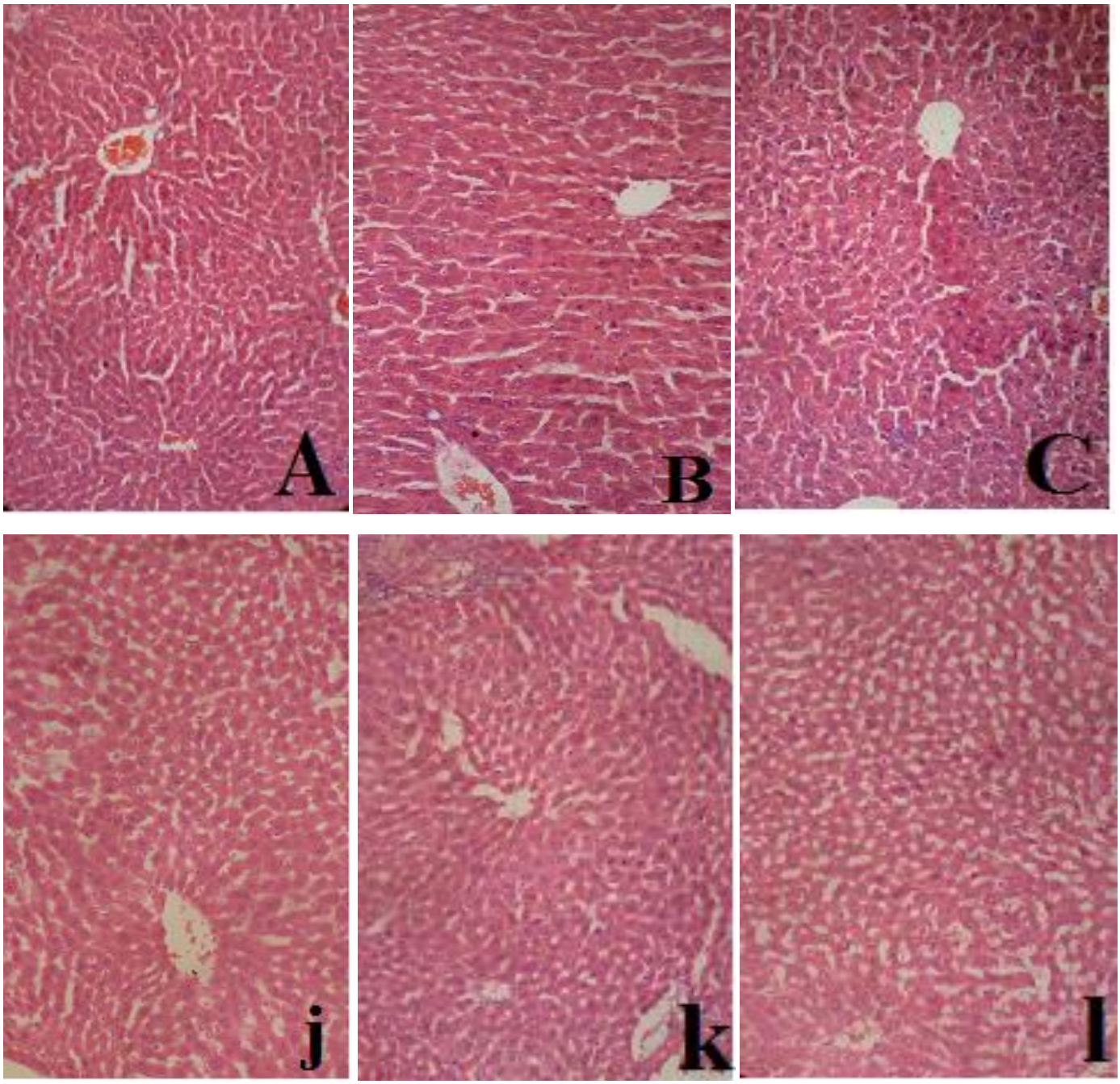

Figure 5. Photomicrographs showing the effect of silymarin, CCL_4, control group and different doses of trachea extract of *M. paradisiaca* on mice liver. **A**: liver section of standard drug silymarin (25 mg/kg) treated group; **B**: liver section of CCL_4 (2.0 g/kg) treated group. **C**: normal control group receiving normal saline (2 ml/kg); **J**: methanolic extract of trachea (100 mg/kg) treated group **K**: methanolic extract of trachea (250 mg/kg) treated group **L**: methanolic extract of trachea (500 mg/kg) treated group (magnification ×10).

(total bilirubin, direct bilirubin, indirect bilirubin, ALP, ALT, AST, serum protein, serum albumin, serum globulin and A/G ratio) and histopathological examinations.

In CCl_4-induced hepatotoxicity model, upon administration of CCl_4 to animals, it undergoes enzymatic activation, majorly by CYP2E1, into the trichloromethyl free radical (CCl_3) within the membrane of the endoplasmic reticulum. This is followed by chloromethylation, saturation, peroxidation and progressive destruction of the unsaturated fatty acid of the endoplasmic reticulum membrane phospholipids. These processes are known as lipid peroxidation, leading

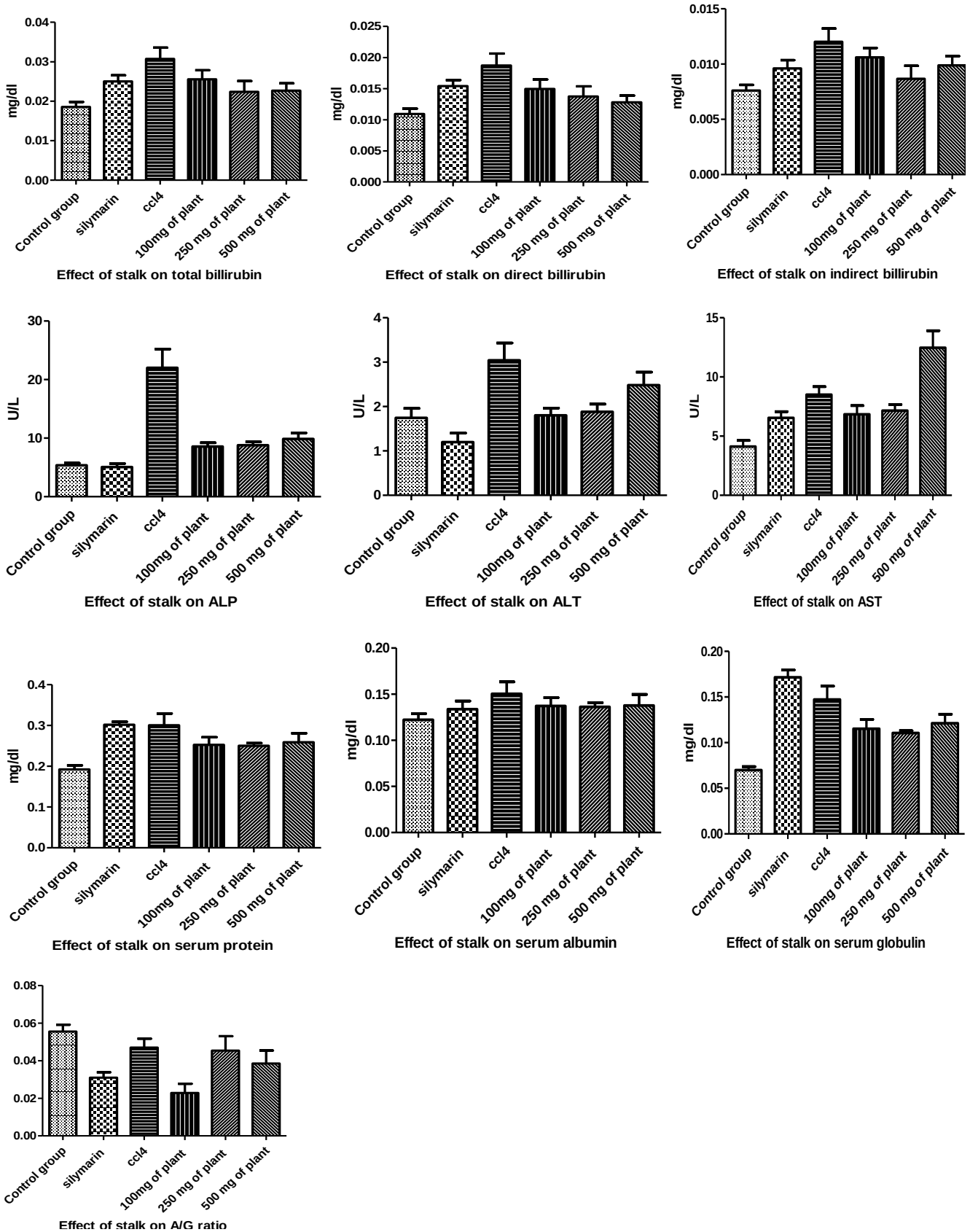

Figure 6. Effect of stalk of *Musa paradisiaca* on liver parameters **(**total bilirubin, direct bilirubin, indirect bilirubin, ALP, ALT, AST, serum protein, serum albumin, serum globulin and A/G ratio).

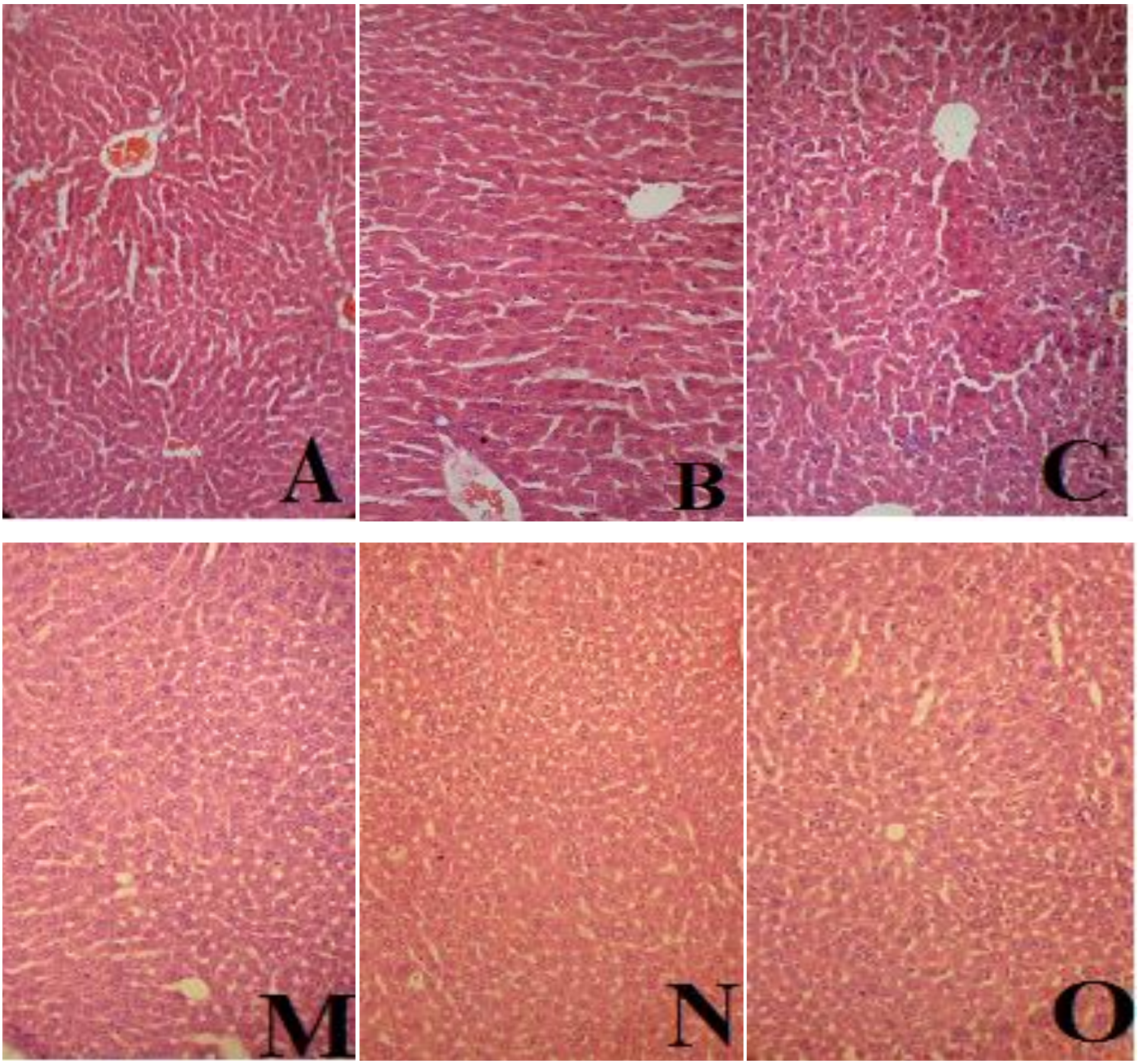

Figure 7. Photomicrographs showing the effect of silymarin, CCL4, control group and different doses of tracheal fluid of *Musa paradisiaca L* on liver histopathology of mice. **A**: liver section of standard drug silymarin (25mg/kg) treated group; **B**: liver section of CCL4 (2.0 g/kg) treated group. **C**: normal control group receiving normal saline (2 ml/kg); **M**: methanolic extract of tracheal fluid (100 mg/kg) treated group **N**: methanolic extract of tracheal fluid (250 mg/kg) treated group **O**: methanolic extract of tracheal fluid (500mg/kg) treated group (magnification 10×).

to functional and structural disruption of hepatocytes. During hepatic damage, cellular enzymes like SGPT, SGOT, ALP, bilirubin (direct and total) leak into the serum resulting in elevation of their serum concentrations (Shenoy et al., 2001).

Measurement of hepatic function markers (SGOT, SGPT, ALP, total bilirubin, direct bilirubin, indirect bilirubin, total protein, serum albumin, serum globulin and A/G ratio) have a clinical and toxicological significance as variation in their values are indications of tissue damage in pathological condition or hepatic dysfunction. Greater amount of release of enzymes from cells are indicative of loss of functional integrity of the cell membrane and cellular leakage and this may be due to abnormal membrane permeability and hepatocyte necrosis (Drotman and Lawhorn, 1978).

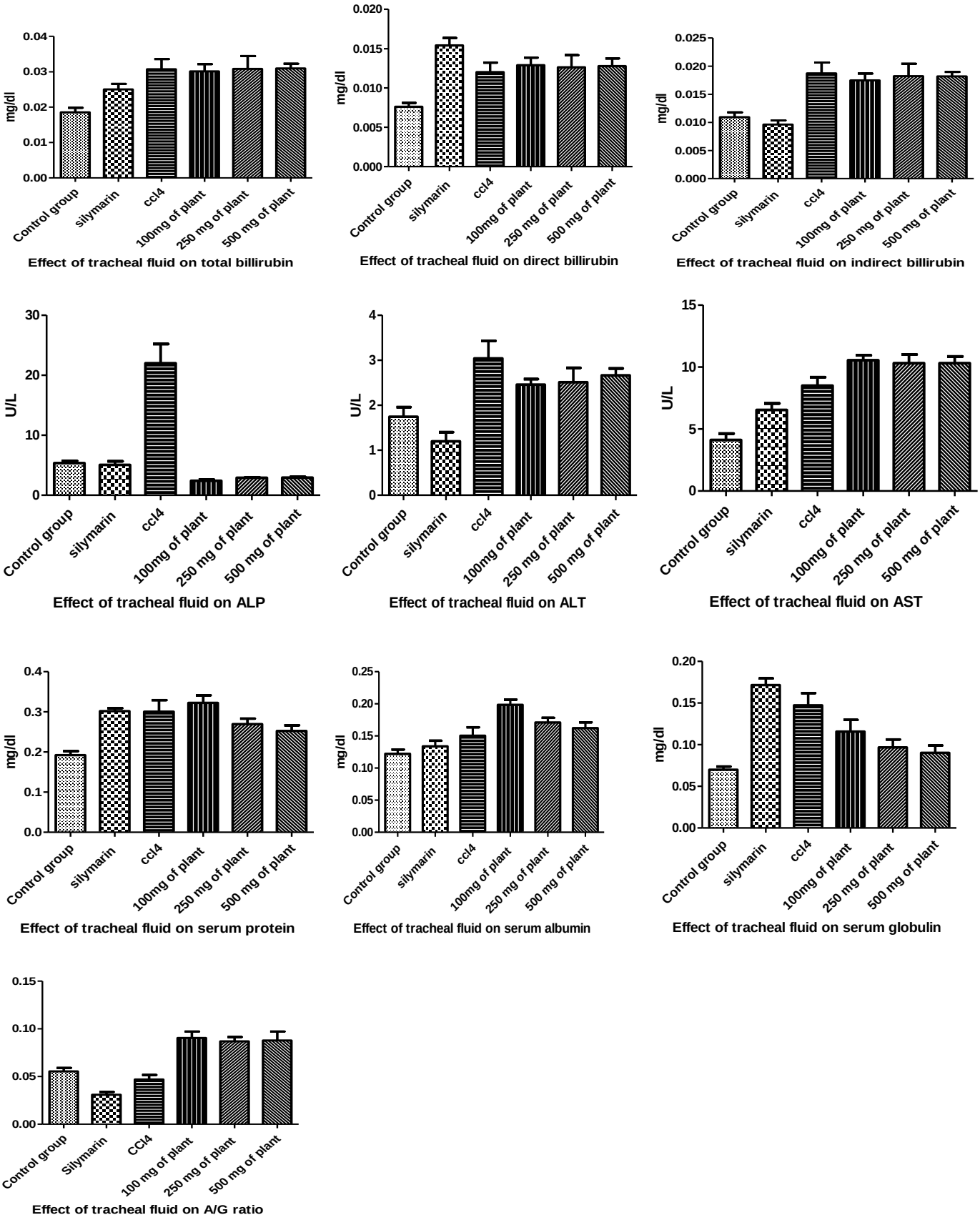

Figure 8. Effect of tracheal fluid of *M. paradisiaca* on liver parameters **(**total bilirubin, direct bilirubin, indirect bilirubin, ALP, ALT, AST, serum protein, serum albumin, serum globulin and A/G ratio).

Conclusion

The result of the present investigation indicates that different morphological parts of *M. paradisiaca* L. such asbracts, flower, trachea and tracheal fluid have potential to cause the hepatotoxicity that depend on the dose and the time duration in experimental mice.

Conflict of Interests

The authors have not declared any conflict of interests.

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Full Length Research Paper

Development of a strategic model of customer relationship management for the pharmaceutical industry of Bangladesh

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Recent academic and practitioner studies have implied that customer relationship management (CRM) provided improved business opportunity yet it has received sundry performance reviews in the present literature. The pharmaceutical industry, in Bangladesh, is in the midst of fundamental changes. Situational regulations have been placed for decades that minimize pressure from competitor companies, and application of modern information technologies that improved the customer knowledge about better service, force the pharmaceutical companies to build relationship with their key customers, such as physicians. This research explored the affiliation among CRM philosophy acceptance, market orientation and relationship marketing, and the subsequent impact on business relationships and relationship performance. A strategic model was developed based on the literature and information obtained through interviews.

Key words: Customer relationship management (CRM), hospital pharmacy, physician.

INTRODUCTION

Pharmaceutical corps, as a very rapid growing sector in Bangladesh and as a part of export industries, to comply with the global competition, has to upgrade themselves and also need to use modern sophisticated strategies. Customer relationship management (CRM) is such a philosophy which helps a company to best deal with its level of customers. To create a framework that estimates the relationship between service qualities attributes, customer satisfaction, retention and loyalty, and to conduct customer segmentation, CRM is a very important tool of modern marketing. Being in institutional regulations and competitive pressure forces, pharmaceutical companies need to adopt customer oriented strategies.

Market orientation in the pharmaceutical sector differs from any other market, as pharmaceutical companies cannot directly sell their products to consumers; rather sales depend on the prescription of physicians and the needs of the patients. In this division, the main customer segments are physicians. However, the patient's

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perspective as the end user of the products should be considered, as sales not only depend on the prescription of physicians but also on the needs of the patients. Severity of disease, cost of buying goods, or socio-economic condition of patients are considered to be significant factors that influence the purchasing of any medication. Hence, the responsibility of the pharmaceutical industry for a contribution to a functioning adequate health system and consumers' access to medicines cannot be spared out. Patients are indirect customers; pharmaceutical responsibility for end user should not only focus on sale/profit, but also economic contribution to health sector improvement. Therefore, a successful pharmaceutical business must arrange its strategy to build a profitable and trustful relationship with physicians. At the same time, it also needs to consider the patients' need as well as socio-economic condition.

CUSTOMER RELATIONSHIP MANAGEMENT (CRM)

Today, marketing must be understood not in the old sense of making sales – "telling and selling" – but in the new sense of satisfying customer needs (Kotler, 2007). Marketing, according to Kotler, is the process by which companies create value for customers and build strong customer relationships in order to capture value from customers in return. Hence, in these modern days, companies are very much interested in building a relationship with customers and maintaining it for long. Customer relationship management (CRM) philosophy comes forward with a view to handling the relationship with customers.

CRM applications, which are relatively new, were visualized for the first time in the 1980s, but only attaining marketing prominence in the late 1990s, primarily due to progresses in information technology, data management systems, better analytics, enhanced communications, systems incorporation and the rapid adoption of the Internet (Berry, 1995). Another commonly used definition is given as: "CRM is an approach or business strategy which provides seamless integration of every area of business that touches the customer" (Bose, 2002). Grönroos (2004) explained that an on-going relationship amid customers will aid in providing a sense of security, trust and feeling of control. Xu and Walton (2005), through studies, have concluded that the key reasons that CRM implemented by corporate managers are as follows:

1. Comprehend customers' needs,
2. Preserve existing customers,
3. Attract new customers,
4. Persuade former clients back into the fold,
5. Reduce customer management costs and increase profits through customer satisfaction.

In pharmaceutical industries of Bangladesh, physicians are considered to be the key customers; major amount of medicine purchase is done by patients according to the prescription written by them. Consequently, physicians' relationship with pharmaceutical companies is the driving force of the industry. The rationale of this research is to explore this relationship.

Specific research objectives

The key relation cascade, in pharmaceutical industry, flows through pharmaceutical companies - physicians - patients. The objective of this thesis is to explore this relationship and its critical factors including:

1. Assessment of physician-patient relationship,
2. Choice of a medicine brand,
3. Handling procedure of customer complaints,
4. Importance of call centers to pharmaceutical-physician relationship,
5. Electronic procedure of collecting and restoring patients' information,
6. Satisfaction of the physicians while prescribing a company's product,
7. Introduction of health insurance may improve service quality to patients,
8. Implementation of e-customer service,
9. Structure IT and analytic keeping with the patient confidentiality and privacy.

Changes are compulsory regarding policy, processes as well as system design. To build up an integrated CRM strategy, this research draws on elements from established business redesign.

Broad objective

To provide the best possible products and services to the customer segments, identify the role and length of relationship with customers, and factors guiding their satisfaction.

RELATED WORKS

According to Zikmund (2000), research could be done either to explore, describe or bestow details of a particular phenomenon.

Exploratory research

Robson (2002) described exploratory research as a valuable means to find out what is happening, to seek new insights, to ask questions to evaluate phenomena in

new light, to generate ideas and hypotheses for future research. Zikmund (2000) on the other hand, defined exploratory research as a lesson conducted to clarify ambiguous problems. According to him, an inquiry for conclusive evidence follows exploratory studies, and it is carried out during the initial stage of the research process; and the initial activities are carried out to refine the problems into a researchable one. According to Samouel et al. (2013), exploratory researches are used to develop better understanding, when there is a little supposition to guide predictions. He further stated by quoting Swaddling and Zobel that "exploratory research presents a system that hooked on consumer perceptions, behaviors, and needs". Moreover, better understanding of customer offers better decision making power and better acknowledgment of market opportunities in favor of companies.

Descriptive research

Descriptive research, according to Robson (2002) is carried out for portraying a precise summary of persons, events or situations. Zikmund (2000) defines descriptive study as one which depicts the characteristics of a population or phenomenon. Samouel (2013) says that descriptive research uses descriptive information, including frequency counts (how many), measures of central tendency like the mean or mode, or quantify variation resembling standard deviation. Solely, the study is exploratory because of the need to find out 'what is happening', to seek fresh insights, to ask questions to evaluate phenomena in new light, to generate and figure out hypotheses about customer relationship in pharmaceutical sector.

RESEARCH DESIGN

The design of the research was developed using the following steps:

1. Questionnaire design
2. Hypothesis

Questionnaire design

There are two crucial objectives of questionnaire design correlated to data quality: First, to diminish non-response, and second, to reduce or avoid measurement errors (Alreck and Settle, 2004).

Questionnaire design process

This is depicted in Figure 1. Information needed for the research has already been clarified in the objective part. In the methodology, the 'interviewing method' has already been illustrated. The question structure is a mixture of 'open ended' and 'close ended' questions. To eradicate complexity as well as wrong meaning, and to

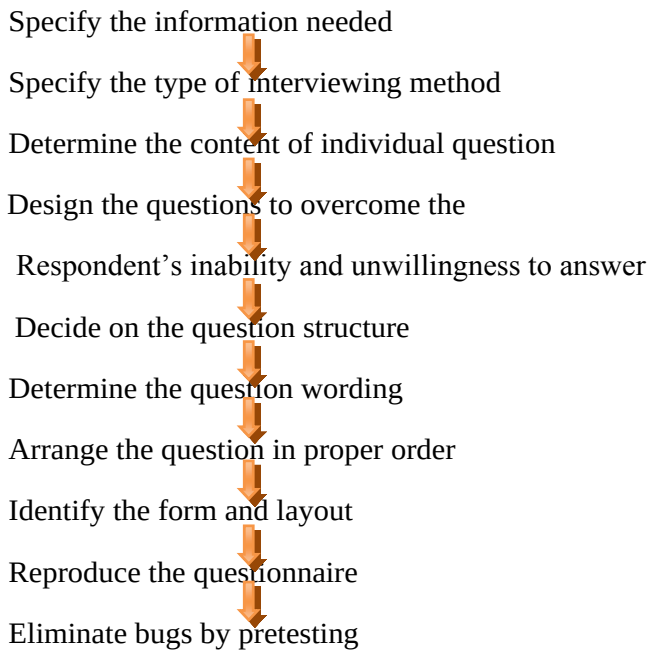

Figure 1. Questionnaire design process (Neresh, 2009).

reproduce the questionnaire, questions are translated from 'English to Bangla' then 'Bangla to English' and are tested for language appropriateness. Finally, pretesting is done with the help of selected samples to eradicate bug in the questionnaire.

Example of questions (questionnaire): How do physicians assess their relationship with patients when they come in contact with patients? Answer choices: a) Very Formal. b) Formal. c) Neither. d) Friendly. e) Very Friendly

Research question

Research question 1 (RQ 1): How do physicians assess their relationship with patients while patients visit them in hospitals?

Research question 2 (RQ 2): Do patients use their judgment to choose a particular brand?

Research question 3 (RQ 3): Do general practitioners grant patients' right to choose medicine brand?

Research question 4(RQ 4): How do physicians handle customer complaints about a pharmaceutical product?

Research question 5 (RQ 5): In hospital areas, pharmaceutical representatives are frequently visiting, how do physicians feel about their movements?

Research question 6 (RQ 6): Are doctors satisfied with various promotional activities of pharmaceutical products?

Research question 7 (RQ 7): Can introduction of health insurance offer better service to customers?

Research question 8 (RQ 8): Do the involvements of electronic

procedures for collecting and restoring information provide better patient care?

Research question 9 (RQ 9): What is the impact of call center on physician-pharmacist relationship?

Research question 10 (RQ 10): What are the Physicians' opinions about the execution of e-customer service?

Research question 11 (RQ 11): What physicians think that online prescription, online appointment service, and online registration to hospitals, physicians and therapeutic search will improve the health sector?

Research question 12 (RQ 12): A pharmacy should be included in every hospital for the elevation of quality of patient care.

Research question 13 (RQ 13): Do physicians think it is essential for the pharmaceutical companies to offer service supports for the specific customer segments?

Hypothesis

The following hypotheses are proposed for Bangladeshi Pharmaceutical Industry based on literature review on CRM.

H1: Patients may be given right to choose his/her medicine brand.

H2: Physicians' views on the implementation of e-customer service.

H3: Physicians' opinion about online prescription, online appointment service, and online registration to hospitals, physician and therapeutic search.

H4: Call center plays a vital role in physician – pharmaceuticals relationship.

H5: To attribute more quality service, hospitals should include hospital pharmacy.

H6: Health insurance will introduce better service to customers.

H7: Movement of representatives in hospitals has significant effect on the CRM.

H8: Electronic procedure of collecting and restoring information about patients may increase the quality of medical service.

Research procedures

The following procedures are included in the research methods.

Scaling

As the research is non-comparative and is designed to measure the attitude of customers, hence, 'non- comparative scaling (Likert scale) technique is selected as a sampling technique Neresh (2009)

Sampling

This involves the collection of elements or objects that possess the information sought by the researcher and about which inferences are to be made (Neresh, 2009). For this research, physicians are conceded as the target population.

Sampling frame is a representation of the elements of target population. It consists of a list or set of directions for identifying the target population (Neresh, 2009). Here, the doctors in Dhaka district are conceded as to be representing sampling frame.

Sampling technique

Quota sampling is selected as sampling technique. Quota sampling may be defined as non probability sampling technique that is a two stage restricted judgmental sampling. The first stage consists of developing control categories or quotas of population elements. In the second stage, sample elements are selected based on convenience or judgment. The only requirement is that the elements selected fit the control characteristics (Neresh, 2009).

In the first stage, quotas of control categories – doctors of Dhaka district are selected. In the second stage, some territories of Dhaka district (based on convenience) are selected as the target population, meaning that the doctors, to be selected as samples, must have to work in selected areas.

Sample size

Total number of Physicians in Bangladesh is 22,120 and the number in Dhaka District is 8,203 (Department of Public Health and Social Service).

Sample size formulas for our sample size determination

$$\textbf{Sample size } (ss) = \frac{Z^2 \times (p) \times (1\text{-}p)}{c^2}$$

Here, Z = Z value (1.96 for 95% confidence level), p = percentage of picking a choice, expressed as decimal, in this case, 20% to response (0.2 used for sample size needed), c = confidence interval, expressed as decimal (for example, 0.05 = ±5). Therefore, ss = 246.

Correction for finite population

$$\text{New ss} = \frac{ss}{1+\frac{ss\text{-}1}{pop}}$$

Where: pop = population=8203. So, final sample size = 239

Interviews and interview guide

In structured interviews, a predetermined or standardized set of questions was asked; whereas in semi-structured interviews order of questions can be varied depending on the flow of conversation (Neresh, 2009).Consider, for example, the following question designed to measure attitude of doctors toward patients:

How do you explain your relationship with patients?
a) Very Formal b) Formal c) Neither d) Friendly e) Very Friendly

This survey method has several advantages. First, the questionnaire is simple to administer. Second, the data obtained are reliable because the responses are limited to the alternatives stated. The use of fixed-response questions reduce the variability in the results that may be caused by differences in interviewers. Finally, coding, analysis, and interpretation of data are relatively simple (Neresh, 2009).

Depth interview is an unstructured, direct, personal interview in which a single respondent is probed by a highly skilled interviewer to uncover underlying motivations, beliefs, attitudes, and feelings on a topic (Neresh, 2009). Churchill and Dawn (2002) suggests that depth interviews suits exploratory research because freedom is provided to the interviewer in conducting the depth interviews and interviewers may try to follow the rough outline, but the order and framing of the questions can be changed. Saunders (2003) says that an interview can be conducted by meeting the person face-to-face or on telephone. “Face to face interviews” was performed for our data collection. Dutka (1995) has mentioned that depth interviews are face-to-face interviews conducted on one to one basis and a detailed discussion outline must be designed. Accordingly, questions must allow the respondents to state whatever thoughts come to their mind. Therefore, due to the nature of research purpose and research questions, there is a mixture of ‘fixed-alternative questions’ and ‘open ended questions’ which have been selected for in-depth face-to -face interview.

RESULTS ANALYSIS

Statistical analysis

Most frequent answers from the physicians of the questions are listed in the Table 1.

Descriptive analysis

The descriptive analysis of the data was undertaken in order to identify any erroneous values.

Reliability testing

The validity of the instrument or questionnaire was first determined using the reliability test by finding out the value of Cronbach’s alpha (Cronbach, 1951) which was found to be reliable. Cronbach's alpha is a measure of internal evenness, that is, how closely related a set of items are as a group. It is a measure of scale reliability. However, a "high" value for alpha does not entail that the measure is one-dimensional. If, in addition to measuring internal consistency, we wish to give evidence that the scale in question is one-dimensional, supplementary analyses can be performed. Exploratory factor analysis is one method of checking dimensionality.

Crosstab analysis

The data collected from the physicians were purely categorical. In Crosstab analysis (Karl Pearson, 1904), dependent variable is doctors’ satisfaction about the promotional activity of pharmaceutical companies (*satisfaction),* which is categorized into 5 categories, respectively: very dissatisfied, dissatisfied, neutral, satisfied and very satisfied. Category neutral is assumed as reference group. Independent variables are relationship of doctors with patient*s (relation)*, patient being given right to choose his medicine brand pharmaceutical companie*s (brand)*, doctors evaluation about the movement of representatives of pharmaceutical companie*s (representative),* introduction of health insurances will improve service qualit*y (insurance)*, electronic procedure of collecting and restoring information of patients may increase quality of patients servic*e (electronic procedure),* call center play a vital role in doctor pharmaceutical company's relationshi*p (call center)*, e-health service will improve satisfaction level of patient*s (e-health)*, hospital should include hospital pharmacy to improve patient servic*e (hospital pharmacy)*, service support for specific customer segment (service), patients choose medicine brand themselve*s (brand choice)*, doctors dealing with complaints of patients regarding pharmaceutical produc*ts (complaints)*, doctors evaluation about using internet by pharmaceutical companies to promote their product *(e-detailing).* These 13 items or independent variables were first found whether they were significantly related to the dependent variable (satisfaction of the physicians) at a confidence level (α) of 0.10% level, using crosstabs analysis. The 7 independent variables identified in the crosstabs analysis were then used in binary logistic regression analysis in order to find which tools used by the industry executives have an impact on the physicians of Bangladesh. The variables that signify in Crosstabs analysis are:

1. Brand.
2. Representative.
3. Insurance.
4. Call center.
5. Age.
6. e-health.
7. Hospital pharmacy

Logistic regression is used to predict a categorical variable from a set of predictor variables.

Multinomial logistic regression

Since Physicians satisfaction about the promotional activity of Pharmaceutical companies (satisfaction) was categorized into five mutually-exclusive groups which carry different implications in customer relationship management (CRM), a multinomial logistic regression was performed to estimate the odds ratio (OR) and 95%

Table 1. Most frequent answers from the physicians.

Question	Most frequent answers	%
Doctor - patient relationship	Friendly	64.5
Patients themselves choose their medicine brands	No	86.5
Patient should be given right to choose a medicine brand	Never	42.5
Physicians evaluation about the movement of representatives of pharmaceutical companies in hospital area	Restricted to a limited area	55.5
Introduction of health insurances will improve patient care	Agree	54
Electronic procedure of collecting and restoring information about patients may increase quality of patients service	Agree	56.5
Call centers play a vital role in doctor pharmaceutical company's relationship	Disagree	41
e-Health service will improve satisfaction level of patients	Agree	47
Pharmaceutical companies should offer service support for specific customer segments	Disagree	39
Hospitals should include hospital pharmacy to improve patient service	Agree	66
Physicians' evaluation about the use of internet by pharmaceutical companies to promote their product	By counseling and consult with the pharmaceutical representatives	68.5
Physicians' deal with complaints of patients regarding pharmaceutical products	According to the patients complaints change the drug or brand	57
Doctors' satisfaction about the promotional activities of pharmaceutical companies	Satisfied	57

Table 2. Neutral vs. Very Dissatisfied.

Doctors satisfaction about the promotional activities of pharmaceutical companies		B	Sig/p-value	Exp(B)/OR	95% Confidence interval for Exp(B)	
					Lower Bound	Upper bound
Very dissatisfied	Brand (sometimes)	-2.890	0.028	0.056	0.004	0.727
	Movement of representative (Neutral)	5.000	0.010	148.413	3.281	6712.770

Reference category is: Neutral

confidence interval (CI) taking 'neutral' as reference category (Greene, 2012). The estimated coefficients and their exponential transformations that yielded the ORs are always relative to the reference category. Thus, the odds of a person with 'satisfied' to 'neutral' is the probability of being satisfied divided by the probability of a person within the neutral category.

Physicians' satisfaction about the promotional activity of pharmaceutical companies

1. In multinomial logistic regression, depended variable is doctors' satisfaction about the promotional activity of pharmaceutical companies (*satisfaction),* which is categorized into 5 categories, respectively: very dissatisfied, dissatisfied, neutral, satisfied and very satisfied.
2. Category neutral is assumed as reference group.
3. Independent variables are patient with given right to choose his/her medicine brand pharmaceutical companies *(brand)*, doctors evaluation about the movement of representative of pharmaceutical companies *(representative)*, introduction of health insurances will improve service quality *(insurance)*, electronic procedure of collecting and restoring information of patients may increase quality of patients service *(electronic procedure)*, call center play a vital role in doctor pharmaceutical company's relationship *(call center)*, e-health service will improve satisfaction level of patients *(e-health)*, hospital should include hospital pharmacy to improve patient service *(hospital pharmacy)*, and age.
4. In the table, p-value ≤0.05 is accepted.
5. Variables that satisfy the condition and signify are brand, representative, insurance, and call center.

Interpretation

In Table 2, regarding categories Neutral vs. Very dissatisfied, the estimated value of B = -2.890 (for brand), which implies that the estimated change in the logit/log-odds is -2.890 and odds ratio (OR) or Exp (B) for very

Table 3. Neutral vs. Dissatisfied.

Doctors satisfaction about the promotional activities of pharmaceutical companies	Independent variables	B	Sig/p-value	Exp(B)/ OR	95% confidence interval for Exp(B)
Dissatisfied	**Insurance**				
	Disagree	2.708	0.022	15	1.475 - 152.492
	Neutral	3.807	0.014	45	2.160 - 937.321
	Agree	2.113	0.050	8.276	0.999 - 68.553

Reference category is: Neutral

Table 4. Neutral vs. Satisfied.

Doctors satisfaction about the promotional activities of pharmaceutical companies	Independent variables	B	Sig/p -value	Exp(B)/OR	95% confidence interval for Exp(B)
Satisfied	**Brand**				
	Often	2.565	0.050	0.977	0.977 - 172.947
	Call Center				
	Strongly disagree	-23.375	0.000	7.055E-11	1.835E-11 - 2.713-10
	Disagree	-22.522	0.000	1.6555E-10	6.386-11 - 4.291E-10
	Neutral	-23.316	0.000	7.478E-11	2.572E-11 - 4.291E-10
	Agree	-21.403	0.000	5.066E-10	5.066E-10 - 5.066E-10

Reference category is: Neutral

dissatisfied category is 0.056 than neutral category, this means the very dissatisfied category have 94.4% lower support to give patients “sometimes” right to choose his/her medicine brand than the neutral category. Exp (B) =148.413 (movement of representative), implies that the very dissatisfied category 148.413 times more neutrally reacts to the movement of representatives than the neutral category. It is clear from the interpretation that physicians in Bangladesh are more interested to prescribe the medicine brand themselves than to give patients flexibility to choose brand. Besides, doctors are very dissatisfied about the movement of the representatives in the hospital areas.

In Table 3 regarding categories Neutral vs. Dissatisfied, the lowest value of B = 2.113 (for insurance), which implies that the estimated change in the logit/log-odds or odds ratio (OR) for dissatisfied category is 2.113 than neutral category and Exp (B) =8.217, shows that the dissatisfied category 8.217 times more agree to introduce insurance for the improvement of the health service to the patients than neutral category.

In Table 4, regarding categories Neutral vs. Satisfied, the value of B = 2.565 (brand), which implies that the estimated change in the logit/log-odds or odds ratio (OR) for satisfied category is 2.565 when the change in neutral category is 1 and Exp (B) =0.977 shows that satisfied category’s support about how ‘Often’ patients may be given right to choose his/her medicine brand is 2.3% lower than neutral category. Values of (B) = -21.403, -22.522, -23.316, -21.403 (for call center) and Exp (B) was almost zero, which implies that the satisfied category has shown its view on call center very much lower than neutral category. It is obvious from the interpretation that physicians who are satisfied about the activities of representatives of pharmaceutical companies are less likely to grant patients’ right to choose medicine brand than physicians who show neutral view about the movements of representative. It is also seen that satisfied physicians are less interested about the opening of call center for patient service.

In Table 5, regarding categories Neutral vs. Very Satisfied, values of (B) = -32.749, -33.916,-33.333,-32.749 (for representative) and Exp (B) is almost zero which implies that very satisfied category has shown its view on call center very much lower than neutral category. It is obvious that very satisfied physicians are less interested about the opening of call center for patient service.

Hypothesis test

Therefore, from aforementioned result of the analysis we can draw the conclusion that the following 4 hypotheses are tested to have significant effect on the physician’s satisfaction:

Table 5. Neutral vs. Very Satisfied.

Doctors satisfaction about the promotional activities of pharmaceutical companies	Independent variables	B	Sig/p-value	Exp(B)/OR	95% confidence interval for Exp(B)
	Representative				
	Movement strictly restricted	-34.314	000	1.252E-15	1.362E-17 - 1.151E-13
Very satisfied	Movement restrict to limited area	-33.916	000	1.864E-15	9.296E-17 - 3.736E-14
	Neutral	-33.333	000	3.338E-15	8.744E-21 - 1.274E-9
	Satisfied	-32.749	000	5.986E-15	5.986E-15 - 5.986E-15

Reference category is: Neutral.

1. Brand.
2. Insurance.
3. Call center.
4. Movement of representative.

DISCUSSION AND OUTPUT MODEL

Regression model

The Block 0 output is for a model that includes only the constant (or intercept). Given the base rates of the two decision options (13% were dissatisfied, and 57% were satisfied), the Hosmer and Lemeshow chi-square test (Hosmer and Lemeshow, 2013) of goodness of fit is the recommended test for the overall fitness of a binary logistic regression model. Since the H-L goodness-of-fit test statistic for the model is 0.685 (greater than 0.05), the zero hypothesis that there is no difference between observed and model-predicted value, is rejected. In other words, this implies that the model's estimate fit the data at an acceptable level.

An omnibus test of model coefficients (an alternative to the H-L test) gives a Chi-Square of 145.110. Under model summary the -2 Log Likelihood statistics is 71.991. The Cox and Snell R^2 (0.222) can be interpreted like R^2 in a multiple regression. In other words, this model explains 22.2% of the total variation of the independent variable (satisfaction of the physicians). From the variables in the equation output, the following variables or predictors were identified to be significantly affecting the dependent variable (physicians' satisfaction which leads to prescribing the company's product):

1. Brand
2. Insurance
3. Call center
4. Movement of Representative

These elements are shown in the output model. Figure 2 illustrates a correlated satisfaction of physicians with brand, insurance, call center, and representative. From the figure, it is clear that four hypotheses (earlier mentioned) are shown to be effective tools for CRM of Bangladeshi Pharmaceutical market. Therefore, following hypotheses are proven by regression model as crucial elements of CRM for Bangladeshi Pharmaceutical Industry:

H1: Patients may be given right to choose his/her medicine brand.
H4: Call center plays a vital role in physician – pharmaceuticals relationship.
H6: Health Insurance will introduce better service to customers.
H7: Movement of representatives in hospitals has significant effect on the CRM.

From the regression model obtained, the following specific research objectives have been answered as well:

1. Determine how a medicine brand is chosen.
2. Evaluate the importance of call centers to deal physician – pharmaceutical company relationship
3. Evaluate the satisfaction of the physicians with a company's product.
4. Introduction of health insurance to provide better service to patients.
5. Evaluate the movement of representative in hospital area.

Strategic model

Without planning, strategic decisions are not possible. Planning is something that throws spotlight on goals, finds the limitations and finally determines an extensive way to achieve the goal. Recent academic and practitioner studies imply that CRM provides improved business opportunity, yet has received sundry performance reviews in the present literature. In addition, the firm's market and technology orientation was considered vital antecedents to the development of CRM strategic model. Therefore, a strategic model for Bangladeshi Pharmaceutical market can be developed as in Figure 3.

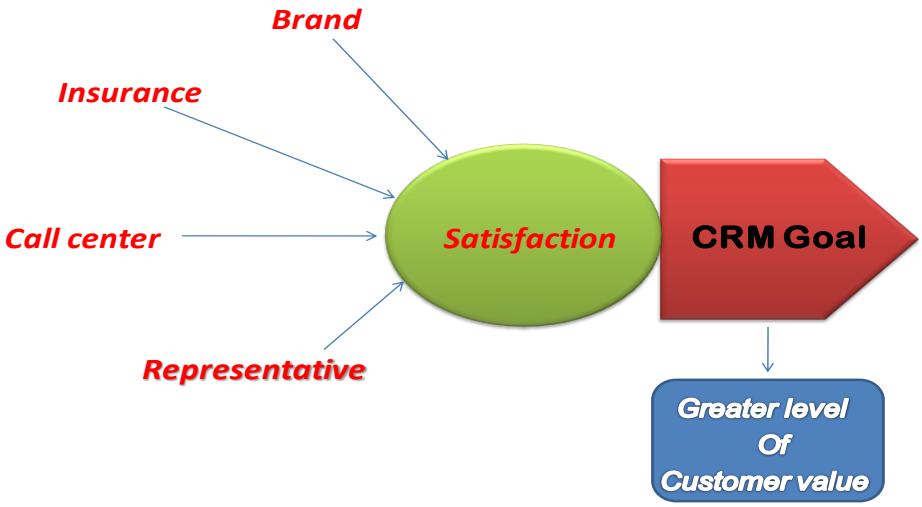

Figure 2. Satisfaction and parameters that affect satisfaction.

Conclusions

Scholars throughout the world have profound attention towards the methods of CRM. The number of organizations, which are adopting customer-centric strategies, programs, tools, and technology for efficient and effective customer relationship management, are increasing day by day. Their key concern is the need for in-depth and integrated customer knowledge in order to build close cooperative and partnering relationships with their customers. The materialization of new channels and technologies (like e-marketing) radically alter how companies interface with their customers, a development which brings about a greater scale of integration between marketing, sales, and customer service functions in organizations. For practitioners, CRM symbolizes a consolidate method for developing full-knowledge regarding customer behavior (Parvatiyar and Sheth, 2000).

Accordingly, the future of CRM technology signals indispensable improvements in CRM systems, which would be able to progress electronic and direct marketing programs, enhance prediction models, improve planning systems of the project resources and transform the agenda and the organizational culture (Baran, 2008, pp. 474-488).

The pharmaceutical industry in Bangladesh is in the midst of fundamental transformation. With the advent of different sophisticated equipment and communication devices, the application of modern information technologies become a very important means to deal with customers. Moreover, improved customer knowledge about better service force and increased competition, forces the pharmaceutical companies to build relationship with their key customers, such as physicians. The affiliation among CRM philosophy acceptance, market orientation, and relationship marketing are explored in this research.

A conceptual model was developed based on the literature and information obtained through interviews. The model incorporated key relationship constructs: trust, vow and interaction quality; and investigated the impact of CRM strategy adoption on these relationship performances. The research consisted of CRM tools development stage, creating, testing and finalizing the research apparatus, followed by a qualitative study of customer's satisfaction. The model applies to Bangladesh, respectively for the regions where the questionnaire interviews were performed.

LIMITATIONS OF THE RESEARCH

Due to time constraint, pharmaceutical marketing personals could not be interviewed, that also have given a better weight into the mode. While assessing questions, respondents' failure to understand the premise of questions, inappropriate or misleading answers, and error during data input might have impeded the appropriateness of the results.

A potential methodological limitation was the small sample size; making the study prone to Type II error. Thus, the statistical tests might have failed to detect significant relationship. Furthermore, the data collected was limited to the time frame given to complete this research. The measurement items and relationship constructs might be imperfect; there might have additional variables which could have been included in the

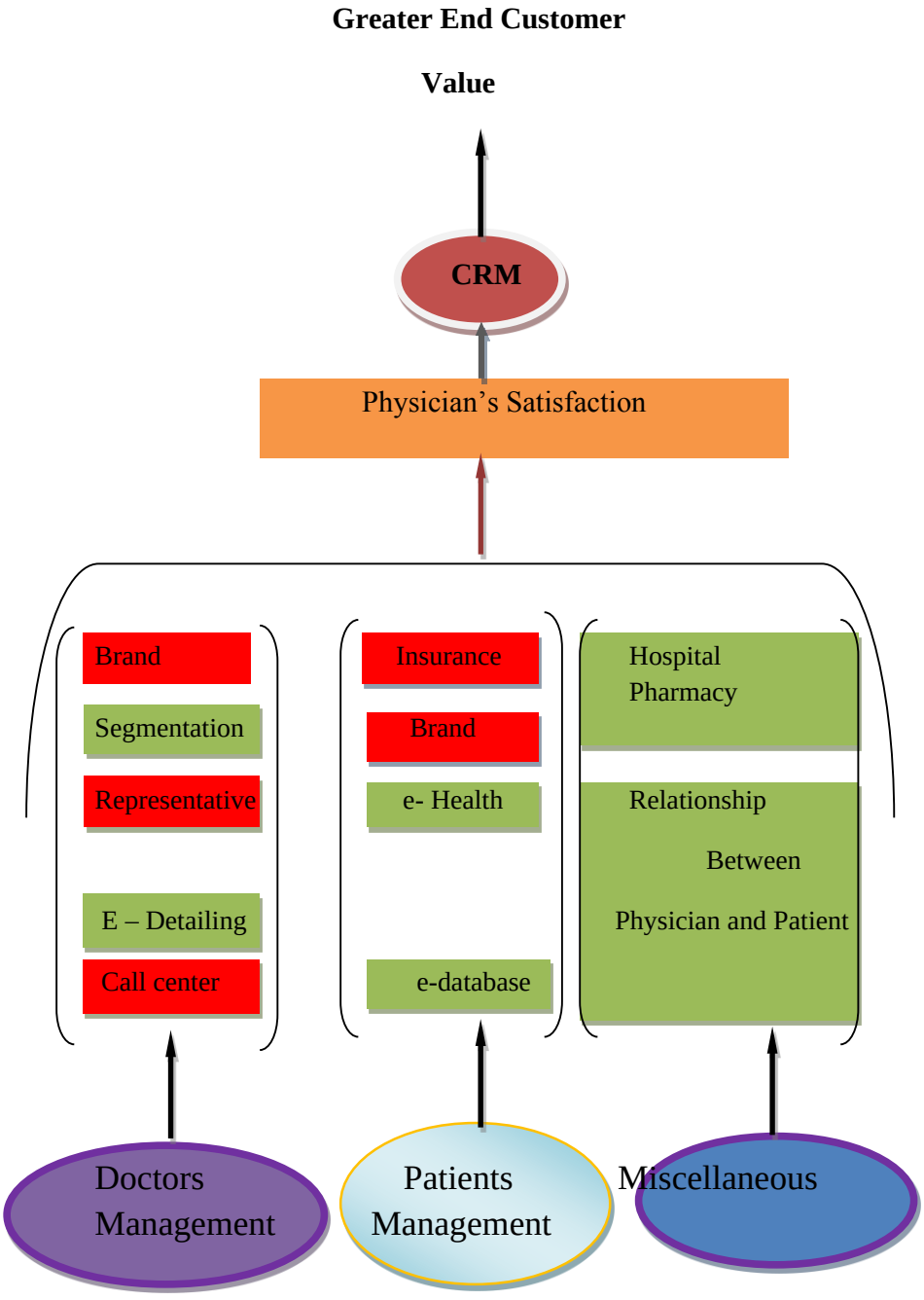

Figure 3. Strategic Model of CRM in Pharmaceutical Industry. The red boxes signify the SPSS model. The green boxes though did not signify, were identified from secondary data.

measurement of satisfaction.

The present research focused only on getting a snapshot CRM in Bangladeshi Pharmaceutical market, and the study tried to construct a CRM model after testing hypotheses. In the broad process of CRM, some of the identified variables, such as market orientation, or customer satisfaction should be expected to change over time and across firms.

Scope for future researches

This study is exploratory in nature. The motives for this study are the relative novelty of the objects of the study (CRM initiatives) and the relative lack of strategic premise to describe such initiatives. Hence, there are still bounties of untapped research opportunities. With growing attentions and momentous investments being made in

CRM systems, several empirical opportunities will emerge. The combination of marketing and information provide a lot of opportunities for research and the results of this study have opened a number of avenues for further investigation. An additional research can be conducted to explore the regional barriers in Bangladesh that are impeding and/or slowing down the speed of CRM maturity. More so, since the current study was conducted in Dhaka division of the country, it might be a good idea to use the proposed model to further assess CRM maturity in other region of the country. Finally, the research can also be carried out using specific groups of specialized physicians.

Conflict of Interests

The authors have not declared any conflict of interests.

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APPENDIX

Appendix A1: Set of questions

1. How do you explain your relationship with patients?

2. Do patients choose their medicine brand?

3. Should patient be given right to choose his/her medicine brand?

4. How do you deal with customer complaints regarding quality and availability of pharmaceutical products?

5. What is your evaluation about the movement of pharmaceutical representatives in hospital areas?

6. Are you satisfied with the promotional activities of pharmaceutical products?
7. Will Health Insurance introduce better service to customer?

8. Do you think electronic procedure of collecting and restoring information of patients may increase the quality of medical service?

9. Do you think call center play a vital role in physician-pharmacist relationship?

10. Please give your views on the implementation of e-customer service?

11. Do you think online prescription, online appointment service, and online registration to hospitals, physician and therapeutic search will improve the health sector?

12. To attribute more quality service, hospitals should include hospital pharmacy.

13. Do you think it is essential for the pharmaceutical companies to offer service supports for the specific customer segments?

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