Chapter – 1

Introduction

Introduction

1.0 Preface

The chapter covers the introduction and an overview of generic medicines including its relevance, classification, distinction amongst innovator's brand, branded generic and generics. Price comparison of few leading products has been included providing information on the substantial price advantage generics offer. The size of the generics market and its growth potential including the drivers of growth has been captured. The crux of the issue, doctors' low acceptance of generics specially in the private sector limiting its mass use has been covered with a rationale to conduct of the study.

1.1 Importance of generic medicines

Generic medicines play a vital part in bringing down the cost of treatment as they are less expensive choices compared to the originators' brand or brand-name alternatives. After an innovator's patent expires, generics are introduced on the market. The world over the generic drugs are being promoted, in India doctors are being directed by the regulatory bodies to write prescription in generic names. The importance of generics has been growing both in the developed and developing nations. The accessibility and preference of generic medicines over brand name drugs bring cost savings in healthcare management. The use of generics is all the more critical specially in countries such as India where out-of-pocket expenditure (OOPE) towards purchase of medicines by patients is one of the highest in the world, besides, most of the Indian population lives in non-urban areas where accessibility & affordability are other major challenges. It is not only patients who are benefitted with the use of generics but also

provides a respite to policy makers in effective managing increasing healthcare budgets.

1.2 Definition & classification of generic drugs

Generic medicines (copies of innovators' brand) are those which are mostly manufactured by companies other than the one which researched the molecule and introduced in the market after the patent expiry of an innovator product.

The commonly understood terms "generic drug" or "generic medicine" meaning a pharmaceutical product which does not require an authorization from an innovator company to manufacture and is marketed after the patent has expired. Generic medicines are usually interchangeable with an original product of an innovator (FDA, 2018; WHO, 2021). The original medication and its generic are identical but have huge price difference. The terms "medicine" or "drug", "doctor or "medical practitioner", "chemist or "pharmacist" are commonly used interchangeably.

Pharmaceutical product contains a chemical substance termed as *Active Pharmaceutical Ingredient* (API) which cures the disease. Some products contain more than one active ingredient.

WHO issued a resolution to help member countries in developing drug policies in 1975 during the World Health Assembly (Alfonso-Cristancho et al., 2015). Many countries since then developed their national drug policies based on the recommendations of WHO (Laing et al., 2003) which lay focus on improving access to essential medicines. WHO essential medicines list (WHO, 2022) includes most effective, safe and inexpensive medicines for urgent circumstances. The major being the generic

medicines which are off-patent and priced much lower as compared to the product of the originator, providing reduction in cost of treatment for patients and healthcare system.

USA Food and Drug Administration (USFDA), the government body regulating pharmaceutical products in USA, has stated that as far as bioequivalence, strength, form, dose, route of administration, safety, efficacy, and intended use are concerned, a generic drug is the same as its original counterpart.

European Medicines Agency (EMA), the pharmaceutical regulatory authority in the European Union(EU), defines a generic drug which corresponds to the reference drug in composition, form and bioequivalence.

1.3 Distinction amongst innovators' brand, branded generic, generic

The terminology of medicine in generic and brand name is different in USA & India. In USA, there is only one brand (innovator's brand) for a particular drug molecule until patent protection period. On expiry of patent, manufacturing & introduction as a generic product is allowed. A branded medicine may have several generic versions. Generic name is the molecule or salt name.

In India, generic medicines are marketed under a brand name known as *branded generics* as commonly prevalent practice originated with a lineage to erstwhile General Agreement on Tariffs & Trade (GATT) which had not so well-defined patent protection laws under Intellectual Property Rights (IPR) giving a leeway under the process patent for introduction of product covered under the patent. The IPR laws were strengthened with well-defined "product" patent protection devoid of any

misunderstanding in interpretation of "process" patent with the evolution of World Trade Organization (WTO) and universally followed by all its members. However, the practice of branded generics continues by the pharmaceutical companies in India where original brands (innovators' product) and branded generics (introduced post patent expiry) are promoted to medical practitioners for their support in prescribing of their brands. Few branded generics are being offered at heavy discounts to pharmacies who push them at the counter as generics. These branded generics can be viewed as brands. There are several branded generic products of the same drug molecule in India unlike one brand and several generic versions in USA. *In addition to GSK's original research molecule - amoxicillin plus clavulanic acid of which Augmentin is the brand name, several other brands, known as branded generics, are also available on the Indian market with the same medication such as Bactoclav (Micro Labs), Novaclav (CIPLA) and others.*

Generics are also available without the brand name but with the chemical or salt name stated on the packs as per the practice followed in the western countries such as USA, UK and others. Government of India under the program PMBJP (Pradhan Mantri Bhartiya Jan Aushadhi Pariyojana) introduced generics (without the brand names) which are available at network of Jan Aushadhi Kendras (exclusive generic drug stores).

With an objective to increase access to affordable medicines, through its initiative PMBJP government of India introduced generic medicines in the Indian market in 2008 at the dedicated outlets known as Jan Aushadhi Kendras. The medicines available at Jan Aushadhi stores are differentiated as distinctively identifiable generics

meaning there is a generic name of medicines printed on the packs without the brand names and the manufacturing and its distribution is managed through the government nominated department, Pharma & Medical Bureau of India (Jan Aushadhi, 2022)

1.4 Cost benefit of generic drugs

The usage of generic medicines is to lower costs and enhance accessibility to affordable healthcare, but quality of generic drugs available in many developing countries differ because of not so well-defined regulatory requirements stressing the need for stringent quality and safety evaluation for generic drugs with an aim to accomplish the goals (Nardi et al., 2014; Bate et al., 2010).

Prices of pharmaceutical raw materials (APIs) and finished dosage forms in India are fixed by National Pharmaceutical Pricing Authority (NPPA). 851 medicines including 4 medical devices are regulated till June 2018 as per the revised Schedule – 1 of National List of Essential Medicines. Price approval is not required for non-scheduled drugs which are outside the purview of price control. For scheduled (controlled) drugs 16% margin to wholesaler and retailer is fixed whereas for non-scheduled formulations the margin to be decided is left to the companies (NPPA, 2018).

Price comparison of some of the leading brands and their generic alternatives is given in Table 1.1

Table 1.1
Price Comparison – Originator Brand, Branded Generic and Generic

Category	GERERIC NAME (salt composition)	ORIGINATOR BRAND			BRANDED GENERIC			GENERIC (Jan Aushadhi kendra)	PRICE DIFFERENCE		
		Brand Name	Company Name	Price MRP (INR) per Tablet / inj.	Brand Name	Company Name	Price MRP (INR) per Tablet / inj.	Price MRP (INR) per Tablet / inj.	Branded Generic vs Originator Brand	Generic vs Originator Brand	Generic vs Branded Generic
Analgesic	Paracetamol 325mg + Tramadol 37.5 mg Tablet	Ultracet	Janssen	15.93	Ultramol	Aristo	7.29	1.20	↓54.2%	↓92.5%	↓83.5%
	Aceclofenac 100mg Tablet	N/A	N/A	N/A	Zerodol	IPCA	5.15	0.70	-	-	↓86.4%
Anti-infective	Amoxycillin 500mg + Clavulanic acid 125mg Tablet	Augmentin	GSK	20.17	Novaclav	CIPLA	20.17	6.00	↓ 0.0%	↓ 70.3%	↓ 70.3%
	Cefuroxime Axetil 500mg Tablet	Ceftum	GSK	113.15	Pulmocef	MICRO	40.00	12.90	↓64.7%	↓88.6%	↓67.8%
	Azithromycin 500mg Tablet	N/A	N/A	N/A	Torthrocin	Torrent	23.78	14.00	-	-	↓41.1%
Antidiabetic	Metformin and Glimepiride 500mg / 2mg Tablet	N/A	N/A	N/A	Glycomet	USV	11.38	1.60	-	-	↓85.9%
	Insulin 40 IU / ml Injection	Huminsulin	Eli Lilly	157.50	N/A	N/A	-	90.00	-	↓42.9%	-
Drugs for central nerve system	Pregabalin 75mg + Methylcobalamin 750 mcg Tablet	N/A	N/A	N/A	Pregacip M	Cipla	14.85	2.80	-	-	
	Carbamazepine 200 mg Tablet	Tegretol	Novartis	1.56	Zeptol	Sun	1.55	0.80	↓0.6%	↓48.7%	↓48.4%
Drugs for cardio vascular system	Cilnidipine 10 mg Tablet	N/A	N/A	N/A	Cilacar	JB	9.89	1.50	-	-	↓84.8%
	Telmisartan 40mg Tablet	Micardis	Boehringer Ingelheim	36.73	Telma	Glenmark	7.40	1.10	↓9.8%	↓86.6%	↓85.1%
	Olmesartan 20mg Tablet	N/A	N/A	N/A	Olmesar	Macleods	11.46	1.70	-	-	↓85.2%
Erectile Dysfunction	Sildenafil 100mg Tablet	Viagra	Pfizer	527.50	Manforce	Mankind	58.00	2.50	↓ 89.0%	↓ 99.5%	↓ 95.7%

Source of information: Chemists, Jan Aushadhi stores & Online pharmacies

1.5 Importance of generics

One main reason by the government of a number of countries in popularizing generic medicines is to make medicines reasonably priced for masses who otherwise cannot afford to buy costly branded drugs. The important role of generic medicines in reducing the healthcare spending has been well acknowledged for a long time. Multiple studies have confirmed achievement in savings ranging 9 to 89% in developing countries through substitution of originator brands by cheaper generic medicines (Cameron et al., 2012).

WHO health expenditures data discloses in India OOPE was 65% as a proportion of health expenditure against the world average of 20% in 2016. Medicines account for single largest expenditure, share of which in OOPE has gone down to 43% in 2015-16 from 51% in 2013-14. Hence, cost of medicines is an important area to dwell on (Singh et al., 2022).

Doctors perform an important role in recommending medicines for curing medical ailment of patients. It is doctors' decision to prescribe branded medicines or by generic names. Generic medicines are cost-effective. Generic prescribing is being promoted in many countries to reduce the cost of treatment. Doctors in India are being directed by the government to prescribe generic medicines which doesn't seem to be going well with them due to several factors.

Generic drugs sold under different brand names classified as *'Branded Generics'* dominate the Indian pharmaceuticals market. Doctors' prescription support is sought by pharmaceutical companies promoting branded generics which are expensive

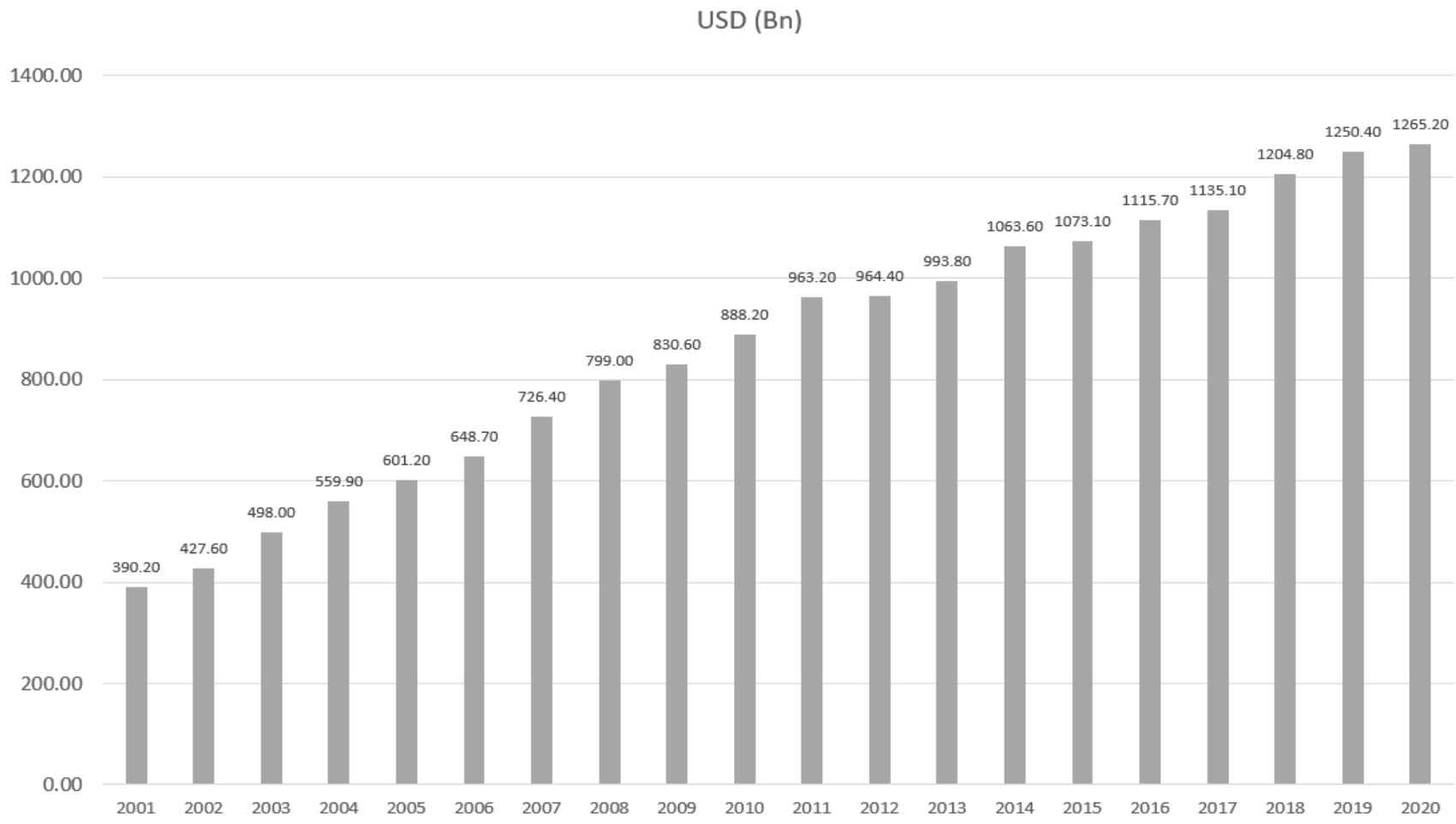
compared with generics sold through the Jan Aushadhi stores. However, few branded generic medicines are being offered to pharmacies at massive discounts making it lucrative for them to substitute prescriptions.

1.6 Trends in use of generics

The global pharmaceutical market has witnessed noteworthy growth in recent years, has grown from $ 390 Bn. in 2001 to $ 1270 Bn. in 2020 growing at Compound Annual Growth Rate (CAGR) of 6.41%.

Globally, USA has emerged as the world's biggest market for pharmaceuticals followed by emerging markets such as Brazil, India, Russia amongst others. However, the lowest share of the global pharmaceutical revenues is the Latin American region.

Global revenue of the pharmaceutical market from 2001 to 2020 is shown in figure 1.1.



Source: https://statistica.com

Figure 1.1 Worldwide Pharma Market 2001-2020

The global generic drug market was worth $ 391 Bn. accounting for 31 percent share in 2020; it was estimated $ 402.9 Bn. in the year 2022 and is projected to reach $ 507.8 Bn. by 2026 increasing at CAGR of 5.6% and $ 575 Bn. by 2030 (Precedence Research, 2022).

USA is also the world's biggest generic drugs market at $ 121.8 Bn. in 2022 accounting for 30.46% share globally. It was in 1984 when the Drug Price Competition and Patent Term Restoration Act, commonly known as *Hatch-Waxman Act*, was enacted in the USA that generic drug promotion came into focus which enabled introduction of generic of the propriety drugs without the requirement of repeating expensive clinical trials. However, bioequivalence studies were made mandatory for approval of generics.

The potential growth in generic medicine market is driven by:

- Lower cost of generics compared to branded drugs
- Rising healthcare treatment cost
- Initiatives / policies of the governments and regulations across the globe
- Acceptance & support from doctors, chemists
- Increasing prevalence of lifestyle and chronic diseases
- Fast paced unplanned urbanization leading to unhealthy lifestyles
- Aging of population
- Pandemic
- Patent expiry
- Awareness amongst population / patients

Humira (AbbVie), Eliquis (Bristol Myers Squibb) and Revlimid (Bristol Myers Squibb) are amongst the top pharmaceutical products in value sold globally. Oncology followed by antidiabetics are amongst the top therapeutic class for drug sales internationally. The areas that have shown the largest growth in healthcare spending in recent years are Autoimmune diseases and diabetes.

Expiry of patented drugs each year meaning losing exclusivity for popular medicines makes it challenging for drug companies engaged in research and development, compelling them to persistently research and introduce innovative drugs to stay afloat. Innovators' drugs whose patent will expire in coming years (Higgins-Dunn, 2022) is shown in Table 1.2

Table 1.2
Patent expiry of innovators' product

Therapeutic Area	Brand name	Company	Revenue in billion USD (2020)	Patent expiry
Diabetic	Humira	AbbVie (Abbott)	19.8	2023
Oncology	Keytruda	Merk & Co.	14.4	2028
Myeloma	Revlimid	Bristol Myers Squibb	12.1	2025-26
Clot	Eliquis	Bristol Myers Squibb	9.2	2027-29
Opthalmology	Eylea	Regeneron, Bayer	8.4	2025-26
Immunology	Stelara	Johnson & Johnson	7.7	2025-26
Oncoloy	Opdivo	Bristol Myers Squibb	7.0	2028
HIV	Dolutegravir	GlaxoSmithKline	6.0	2027-29
Oncology	Ibrance	Pfizer	5.4	2027
Diabetic	Januvia & Janumet	Merck	5.3	2022-23
Diabetic	Trulicity	Eli Lilly	5.1	2027-29
Osteoprosis	Prolia / Xgeva	Amgen	4.6	2025-26
Immunology	Cosentyx	Novartis	4.0	2025-26
ulcerative colitis	Entyvio	Takeda	4.0	2025-26
Diabetic	Victoza	Novo Nordisk	3.0	2022-23

Source: https://www.fiercepharma.com

The rising incidence of chronic diseases is one of the major growth drivers of the generic pharmaceutical market.

1.7 Challenges with generics

The government's directive towards a legal framework to make doctors prescribe generic drugs followed by advisories issued by Medical Council of India (MCI) asking medical practitioners to recommend generic drugs has not gathered full support of doctors largely from the non-government sector. Doctors so far seem unwilling to prescribe generics or chemical / salt names.

There are numerous challenges with generic medicine prescription. The challenges obstructing popularity of generic medicines are due to several factors related to general population, chemists, prescribers, regulations and marketing of branded medicines by pharma companies which are detailed in the literature review.

One major challenge is acceptance of quality of generics by doctors, a proportion of whom are hesitant to prescribe medicines in generic names as they are not sure of effectiveness of generics, besides, safety of generic drugs and their availability are impediment to practitioners' prescription of generics (Colgan et al., 2015; Kamejaliya et al., 2017; Roy & Rana, 2018; Dhale et al., 2020).

Bioequivalence study establishes performance of a generic drug by comparing absorption and its rate in the blood stream at the site of drug action of an API of generics with the original branded medicines. Regulations in generic product registration in India requires bioequivalence studies to be performed on drugs with low solubility. However, the eligibility for bio-waivers include drugs that are highly

soluble in water which are considered to be likely easily absorbed in the body, hence may not require bioequivalence study. There are drugs which are exempted for bioequivalence studies. In the absence of stringent quality enforceable measures like that in USA, doctors in India rely on reputation of a company like CIPLA, Dr. Reddy's Lab, Sun Pharma and others who over the years have demonstrated their commitment to quality (Soans, 2022).

Another challenge is in dispensation of medicines. Prescription in generic drug may get substituted by pharmacists who may dispense generic or his favorite branded generic in which he makes more profit. Some branded generic medications are being offered to pharmacies at substantial discount make it lucrative for them to substitute prescriptions at counters. With such practice how the price benefit of generics can be realized by patients is another challenge.

Knowledge in differentiating original brands, branded generics, generics is inadequate in patients / general population making it harder for acceptance of generics. General belief that anything which is cheap may be inferior in quality may hold true for medicines as well. Moreover, patients tend to buy what doctors prescribe.

Looking at the perspective of pharmaceutical companies, one major challenge is how to promote generic medicines to doctors and get their support for prescription knowing the prescription in generic name may get substituted with another generic of chemist's choice.

Moreover, marketing promotional practices being followed by pharma companies with the engagement of *Medical Representatives* (MRs) who provide product

information and seek prescription support from doctors is leading to branded prescription practices (Aivalli et al., 2018).

How to break the connection between pharmaceutical companies and doctors is another challenge? Promotion of branded medicines has been an established practice by pharmaceutical companies. MRs have played a constructive role in building trust with the doctors. The linkage works either way, product information to doctors and feedback to pharmaceutical companies from doctors. The influence of doctors by pharmaceutical companies makes it challenging for doctors to prescribe generics.

Doctors play an important role in treating their patients by prescribing medicines. Prescribing branded medicines or medicines in generic names is a decision of doctor. The low acceptance of generics by doctors is an important area of research to unearth factors around knowledge, attitude and practice of medical practitioners towards generic drugs with an aim to find research based solution that may lead to mass use of generic drugs.

Knowledge amongst medical practitioners is explored in terms of awareness of generic medicines, its usage, Jan Aushadhi scheme & IMC guidelines, whereas attitude towards generic medicines is explored in terms of beliefs medical practitioners hold in a variety of areas such as effectiveness, safety, reputation of manufacturers amongst others. Practice focusses on areas related to factors that influence prescription practice of doctors such as cost of medicines, promotion by pharma companies, published literature, substitution, socio-economic status of patients amongst others.

The problem in the study is identified in terms of ascertaining the factors that have influence on doctors in prescribing generic medicines and understanding the relationship between factors and prescription of generic drugs.

1.8 Research questions

The research questions framed for the study are included in the Table 1.3.

Table 1.3
Research questions

Sr. No.	**Research Question**
RQ 1	*Does knowledge of generic medicines play a significant role in influencing doctors in prescribing generic medicines?*
RQ 2	*Does attitude towards generic medicines play a significant role in influencing doctors in prescribing generic medicines?*
RQ 3	*Does practice of doctors play a significant role in influencing doctors in prescribing generic medicines?*
RQ 4	*Is there any difference in practice of prescribing generic medicines amongst doctors serving at primary, secondary and tertiary healthcare centers?*
RQ 5	*Does knowledge (cognitive) of generic medicine, attitude (affective) towards generic medicines and practice (conative) have a significant influence on doctors in prescribing generic medicines?*

1.9 Research objectives

The importance of the research study is from the perspectives of society, healthcare providers, pharmaceutical industry and academics. The objectives of this research are…

I. To ascertain factors that have influence on doctors in prescribing generic medicines.
II. To find out relationship between factors and prescription of generic medicines

III. To compare level of influence associated with different factors on doctors at different healthcare delivery points – primary, secondary and tertiary healthcare centers.

IV. To evaluate if acceptance and use of generic medicine could be explained by Tri-component Model of Cognitive-Affective-Conative processes of decision making.

V. To bring forth suggestions that may lead to increase in prescribing of generic medicines.

VI. To suggest marketing aspects of generic medicines that the pharmaceutical companies need to take into consideration based on the outcome of the analysis of the study.

1.10 Chapter Plan

The study is covered in seven chapters as illustrated below:

Chapter 1 Introduction

This chapter covers the introduction and an overview of generics including its relevance, classification, distinction amongst innovator's brand, branded generic and generics. Price comparison of few leading products has been included providing information on the substantial price advantage generics offer. The size of the generics market and its growth potential including the drivers of growth has been captured. The crux of the issue, doctors' low acceptance of generics specially in the private sector limiting its mass use has been covered with a rationale for conduct of the research study.

Chapter 2 Review of Literature

The chapter details review of various research papers, articles and books relevant to this research providing an insight into the issues related to generic medicines with the studies conducted in the world including India covering perspectives of doctors, pharmacies, patients, chemists, government policy, regulation. The research gaps were identified which helped in narrow down the focus in further conduct of the study with a focus on knowledge, attitude and practice of medical practitioners towards generic medicines.

Chapter 3 Materials and Methods

The chapter describes the process followed in research methodology with the development of research design and the procedures for conduct of the study. It specifically illustrates instrument development, administering the instrument, sampling, data collection and analysis procedures, reliability and validity of the instrument.

Chapter 4 Results

The chapter comprises testing of hypotheses with an application of various statistical techniques with the use of SPSS in answering the research questions / testing the hypotheses that were initially developed at the commencement of the study following literature review as refereed in approved synopsis.

Chapter 5 Discussion

The findings are discussed in relation to the study keeping in focus perspective of stakeholders such as doctors, patients, populations, chemists, pharmaceutical companies, government policy and understanding of the issues concerning generic medicines reflects insightfulness into the subject which presents uniqueness of the research. The potential contribution of the research outcome to the subject of knowledge, attitude and practice of doctors towards generic medicines are highlighted.

Chapter 6 Conclusion

Research conclusion as answers to the research questions are presented in the chapter supported with the outcome of testing of hypotheses. Managerial implications, limitations of the study, recommendations and directions for future research are included.

Chapter 7 Summary

The summary of the study is given in chapter 7.