

**Summer Training at
Sun Pharmaceutical Ltd.,
Mumbai**

**A Study on Need and Awareness of Topical Anti-Inflammatory & Analgesic
Gels Containing Higher Concentration Diclofenac**

**By
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**Under the guidance of
Dr. Nirmal Kumar Gurbani**

**MBA Pharmaceutical Management
2015-2017**



**The IHHMR University, Jaipur
2016**

CERTIFICATE

TO WHOMSOEVER MAY CONCERN

This is to certify that **Mr. Adil Refai**, student of MBA Pharmaceutical Management (MBA PM) from The IIHMR University, Jaipur has undergone internship training at **Sun Pharmaceuticals Ltd, Mumbai** from **4th April 2016** to **1st June 2016**.

The Candidate has successfully carried out the study designated to him during internship training and his approach to the study has been sincere, scientific and analytical.

The Internship is in fulfillment of the course requirements.

I wish him all success in all his future endeavors.



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SPIL/COR/HRD/PROJ/16
June 1, 2016

TO WHOMSOEVER IT MAY CONCERN

This is to certify that **Mr. Adil Refai** of Indian Institute of Health Management & Research has undergone her summer project in Sun Pharmaceutical Industries Ltd in **Classic Division PMT Department** from **April 04, 2016 to June 1, 2016**. His project title was **"Study on Perception, Need and Awareness of Topical Anti-Inflammatory and Analgesic Gel containing higher strength Diclofenac among doctors"**. He has completed the project to the satisfaction of his project guide and the organisation.

We wish him success in all future endeavors.

For **SUN PHARMACEUTICAL INDUSTRIES LTD.**

RAVI JAGGI
DEPUTY GENERAL MANAGER – HUMAN RESOURCES

ACKNOWLEDGEMENT:

I take this opportunity to express my profound gratitude and deep regards towards SUN Pharmaceuticals Industries Ltd. for giving me an opportunity to work as a summer Intern in the organization.

First of all I express my sage sense of gratitude and indebtedness to my Organization mentor: **Mr Surinder Pal Singh (SBU Head – Classic division)** and Organization Project Guide: **Dr Chavi Sandhu (Marketing Head – Classic division)** for their exemplary guidance, monitoring and constant help and encouragement throughout the course of my summer internship project.

I would also like to express sincere thankfulness towards all the Sales Executives and Sales officers of SUN Pharmaceuticals (Classic Division) who helped me in accomplishing the field work and granting their valuable time during the course of field work.

I also owe my wholeheartedness thanks and appreciation to each and every member of SUN Pharma (Classic Division) for their kind advice, suggestions and constant help in lot of various ways during my project.

I would also like to thank my Institute IIHMR University, Jaipur which provided me a platform for a precious engagement with SUN Pharmaceuticals in a Summer Internship program.

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Abbreviations:

MSD	Musculoskeletal Disorder
T.A	Topical Analgesic (Anti-Inflammatory)
G.P	General Physician (MBBS)
C.P	Consulting Physician (M.D)
STDev	Standard Deviation
Max	Maximum Value
Min	Minimum Value
O.A	Osteoarthritis
MS	Market Share
RCT	Randomized Controlled Trail
DDEA	Diclofenac Diethyl amine
LBP	Low Back Pain
O.D	Once in a day
B.I.D	Twice in a day
T.I.D	Thrice in a day
Q.I.D	Four times a day
Comb.	Combination

Executive Summary:

PROJECT OBJECTIVES:

❖ Primary Objective:

- To find out the Need and Awareness about higher concentration Topical Anti-Inflammatory & Analgesic Gels among doctors.

❖ Secondary Objectives:

- To understand the prescription behavior of doctors in Topical Anti-Inflammatory & Analgesic gels.
- To understand the Perception's of doctors about Topical Anti-Inflammatory & Analgesic gels

RESEARCH METHODOLOGY:

- **Research Type-** Exploratory Research
- **Data collection tool** - Structured Questionnaire (Open ended & Close ended) & Discussion
- **Sample size** - 101 Doctors
- **Sampling** - Convenience sampling
- **Study area** - Mumbai, India
- **Respondents** - General Physician (G.P - 75) and Consulting Physician (C.P - 26)
- **Analysis tool** - MS Excel 2007

RESULT & CONCLUSION:

a) General Physician (G.P)

- Total number of MSD patients treated per day is **506** (patients/day) by **73** G.Ps, means one G.P on an average treats **6.93 (~7)** MSD patients/day.
- **Minimum** and **Maximum** number of MSD patients treated by a G.P per day is ranges from **0-1** patients/day and **20** patients/day respectively.
- Out of **506** MSD patients treated by **73** G.Ps, **315** are prescribed with Topical Anti-Inflammatory & Analgesic Gels (T.A gels). This implies that G.Ps prescribed **62%** of treated MSD patients with T.A gels
- **100% (71 G.Ps)** of G.Ps prefer Diclofenac & Combination molecule in T.A gels, followed my second most preferred molecule is Capsicum & Combination prescribed by **6** G.Ps, Piroxicam – **5** G.Ps, Mephenesin & Combination – **5** G.Ps, Ayurvedic – **3** G.Ps and others with total **13** molecules responded by G.Ps in T.A gels.
- Most preferred dose by G.Ps in T.A gels is **T.I.D** application with **57%** (Out of (63 G.Ps) 100%) of G.P's preferred dose, followed by **B.I.D** with **37%** of G.P's preferred dose.
- Majority of G.P's preferred duration of treatment with T.A gels is **5-10 days** with **40%** of G.Ps preferring **5-10 days** duration. It is followed by **30%** of G.Ps preferred duration as “**Till Asymptomatic condition**”.
- **Voveran (43% of G.Ps)** is the most preferred brand in T.A gels by G.Ps, followed by **Volini** (16% G.Ps).
- **71%** (40 out of 56) of G.Ps perceives that T.A gels gives improved pain relief in <60% of patients treated with T.A gels.
- **60%** of G.Ps (45 out of 75) suggest that there is no need for higher conc. of T.A gels in market, with reasons for not considering need were **safety(side effects)** – **25%** G.Ps, followed by reasons as “**It just acts as a placebo**” with **22%** of G.P's suggesting it. Also **22%** of G.Ps says “Oral gives better results”.
- Lesser awareness among G.Ps was seen for higher concentration 2% Diclofenac gel with **61%** G.Ps were **not aware** about 2% diclofenac and combination gel.
- Most preferred indications for 2% diclofenac and combination gels suggested by G.Ps is **Severe Pain** (22% of G.Ps), followed by **Low back pain** (18% G.Ps), **Arthritis** (15% G.Ps) etc.

b) Consulting Physician (C.P).

- Total number of MSD patients treated per day is **164** (patients/day) by **25** C.Ps, means one C.P on an average treats 6.5 MSD patients/day (13 MSD patients per two days)
- Minimum and Maximum number of MSD patients treated by a C.P per day is ranges from **1-2** patients/day and **15** patients/day respectively.
- Out of **164** MSD patients treated by **25** C.Ps, **110** are prescribed with Topical Anti-Inflammatory & Analgesic Gels (T.A gels). This implies that C.Ps prescribed **67%** of treated MSD patients with T.A gels, which is slightly higher than G.Ps.
- **100%** (26 C.Ps) of C.Ps prefer Diclofenac & Combination molecule in T.A gels, followed my second most preferred molecule is Capsicum & Combination prescribed by **4** G.Ps, Piroxicam – **2** G.Ps, Ayurvedic – **2** C.Ps, Indomethacin – **2** G.Ps and others with total **11** molecules responded by C.Ps in T.A gels.
- Most preferred dose by C.Ps in T.A gels is **T.I.D** application with **65%** (Out of (20 C.Ps) 100%) of C.P's preferred dose, followed by **Q.I.D** with **25%** of C.P's preferred dose.
- Majority of C.P's preferred duration of treatment with T.A gels is "**Till Asymptomatic condition**" with **50%** of G.Ps preferring the same duration. It is followed by **22%** of C.Ps preferred duration as **1-5 days**.
- **Volini (33%** of C.Ps) is the most preferred brand in T.A gels by C.Ps, followed by **Voveran (28% G.Ps)**. Thus C.P's are potential customers for Volini brand.
- **79%** (15 out of 19) of C.Ps perceives that T.A gels gives improved pain relief in <60% of patients treated with T.A gels.
- Majority, **62%** of C.Ps (16 out of 26) suggest that there is need for higher concentration of T.A gels in market
- **38%** of C.Ps suggests that there is no need for higher concentration of T.A gels in market with reasons for not considering need were **safety (side effects)** – 50% C.Ps, followed by reasons as "**Need Clinical studies**" with **25%** of C.P's suggesting it. Also **12.5%** of G.Ps perceives "**Oral gives better results**".
- **Better awareness among C.Ps** was observed for higher concentration 2% Dicofenac gel with **54%** C.Ps were aware about 2% diclofenac and combination gel.
- Most preferred indication for 2% diclofenac and combination gels suggested by C.Ps is **Arthritis** (18% of C.Ps), followed by **Osteoarthritis** (15% C.Ps), **Low back Pain & Muscular spasm** (13% each) etc.

MARKET RATIONALE:

- Total Pain/Analgesic market is **~8143 Cr** (MAT Value 2015_IMS_Base file)
- Topical Pain/Analgesic market is **~800Cr (9.5%)** of total pain/analgesic market (MAT Value 2015_IMS_Base file)
- **745** brands in Topical pain/Analgesic segment
- Out of the topical pain/analgesic market **59.8%** is R_x market.
- Percentage share of Diclofenac and Combination molecule in Topical pain/analgesic market is **66.7%**. (MAT 2015)
- Topical Analgesic market CAGR (2012-2015) is **12.45%**.

Leading brands in Topical Analgesic segment:

Brand (Formulation)	Company	Market Share (%)	Sales Value (Rs) (Feb'16)	CAGR % (2012-'16)	Product launch	Price (Rs/SKU)
Volini	Sun	31%	240.7 Cr	9%	1994	90/ 30gm
Moov	Reckitt Benkiser	6%	43.3 Cr	14%	1997	75/ 25gm
Voveran	Novartis	5%	40.5 Cr	9%	1992	86.75/ 30gm
D.F.O	Ozone	3%	22.3 Cr	20%	2001	79/ 30gm
Oxalgin	Zydus	3%	21.7 Cr	10%	2009	90/ 30gm
Dynapar QPS (Solution)	Troikaa	2%	17.1 Cr	91%	2013	197 / 30ml
Volitra	Sun	2%	17.0 Cr	3%	2007	83/ 30gm

NEW PRODUCT RATIONALE:

Ingredients	Mechanism of action	Potential therapeutic application
Diclofenac Diethyl amine (2.32%w/w)	Inhibition of COX enzyme	Reduces Inflammation & Pain
Methyl Salicylate (10%)	Causes dilation of capillaries	Reduces Pain sensation
Menthol (5%)	Counter irritant, Cold TRPM8 sensitization	Reduces Pain sensation & provides Cooling effect

RECOMMENDATIONS:❖ **Targeting & Segmentation:**

- Our potential targets should be General Physician (**G.P**) and Consulting Physician (**C.P**) along with others specialties (Gynaec, Rural and Ortho). (Diclofenac Gel R_x share is G.P+C.P = 34% R_x share among all specialties – SMSRC R_x data)
- Segmentation of area: 1) Metro Cities 2) Class A town 3) Class B town (Because higher population can be covered)

❖ **Marketing Mix:**

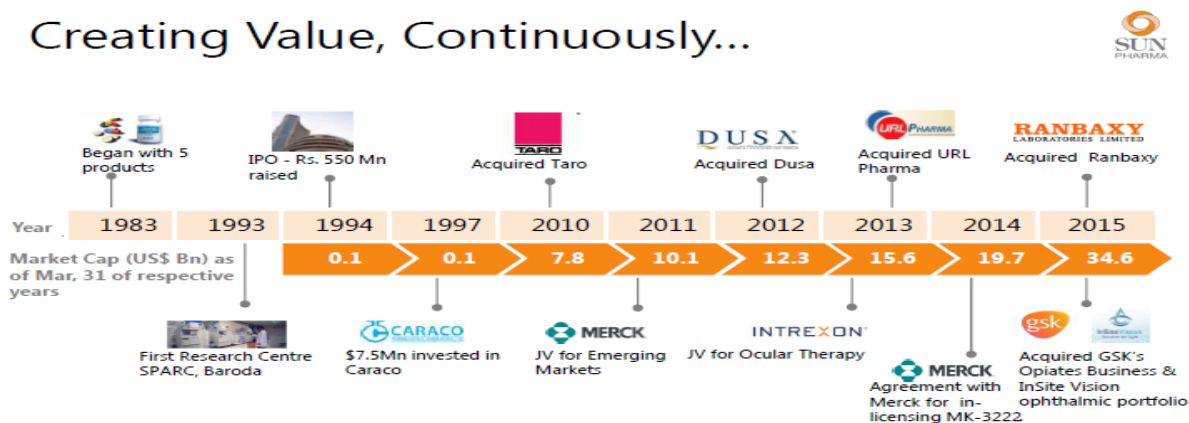
- **Product:** Novelty factors would be higher concentration 2% Diclofenac gel with B.I.D application advantage and lesser side effects than Oral Diclofenac (Quotations supported by Clinical studies).
- **Promotion:** Awareness needs to be created among G.Ps and C.Ps, special focus on G.Ps as G.Ps have lesser awareness about 2% Diclofenac and combination Gel, this will help to create the demand (Need). Clinical Studies and Human trial data should be distributed and important statements of product promotion should be backed by Clinical studies. Separate promotogram has to be made for both G.Ps and C.Ps
- **Pricing:** Value based Pricing must be adopted (Which is providing quality product at a fair price, as G.Ps and C.Ps are more sensitive towards price change and premium price)
- **Packaging:** Similar packaging as Volini should be adopted with slight changes as per requirements (Helps in retaining Brand loyal customers), PIL necessary in every pack unit.
- **Positioning:** Product should be position for Acute indications (Low back Pain, Knee pain, Joint Pain) to G.Ps and for Chronic Indications (Arthritis, O.A, Injury, Severe Musculoskeletal Pain) to C.Ps. (As per suggestions given by specialties)
- **Others:** Create our own PSUR (for monitoring Safety of product during first six month of launch. This will help in reflecting responsibility towards society).

Company Profile:

Sun Pharma pioneered specialty marketing in the Indian pharma industry when the company began in 1983. Today, company has reached leadership in each of the therapy areas that they operate in, and have built a reputation of trust and quality with their customers.

SUN PHARMA JOURNEY FROM 1983 TO 2015:

Creating Value, Continuously...



Sun Pharma Today



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Sun Pharma at a glance

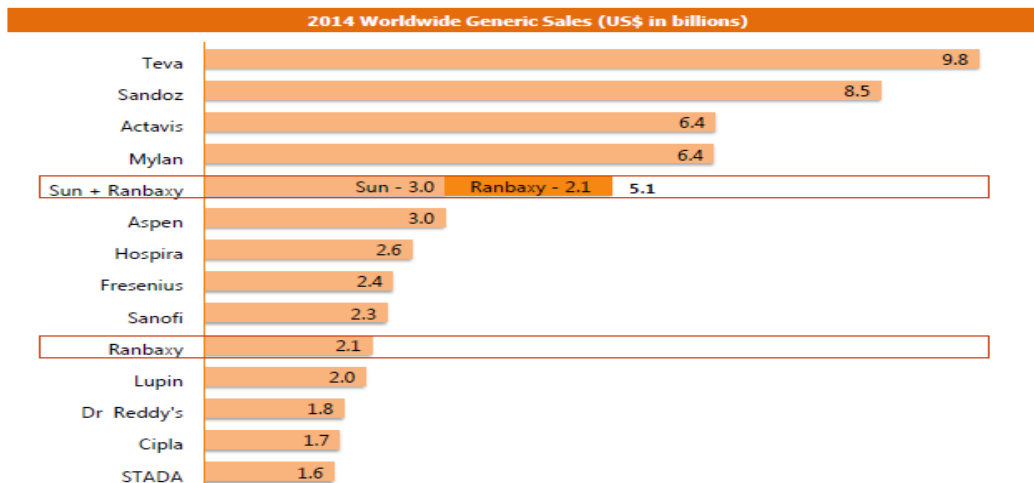
5 th Largest Global Specialty Generic Company	
US	• Ranked 5 th in US* / Largest Indian Pharma Company in US
India	• No. 1 Pharma Company in India
Emerging Markets	• Largest Indian Pharma Company in Emerging Markets
Europe	• Expanding presence in Europe
Manufacturing Footprint	• 50 manufacturing sites across the world
Market Presence	• Presence in more than 150 countries across branded and generic markets
Product Portfolio	• Portfolio of more than 2,000 products across the world
Employees	• 30,000+ global employee base
Quality Compliance	• Multiple facilities approved by various regulatory authorities across the world including USFDA
R&D and Manufacturing	• Capabilities across dosage forms like injectables, sprays, ointments, creams, liquids, tablets and capsules
Addressable Segments	• Specialty products, branded generics, complex generics, pure generics & APIs

* Source: Evaluate Pharma for 12 months ended Dec 2014

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World's 5th Largest Specialty Generic Pharma Co



Source: Evaluate Pharma, Company filings

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Sun Pharma today

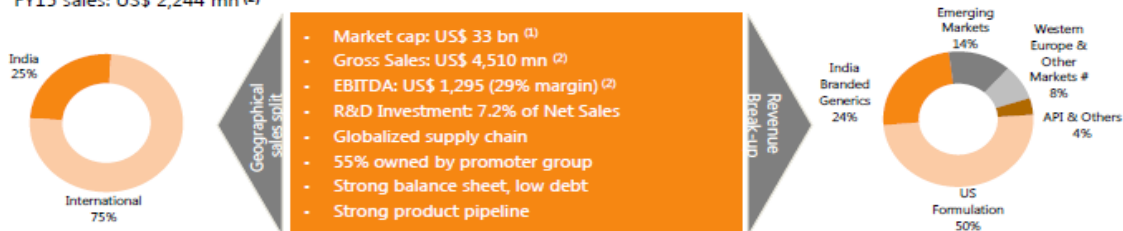


US Formulations

- 5th largest generics company in US* with one of the largest ANDAs pipeline (154 ANDAs awaiting approval)
- Presence in generics, Specialty and branded segments with more than 440 approved products
- FY15 sales: US\$ 2,244 mn ⁽²⁾

India Branded Generics

- No.1 ranked with 13 classes of doctor categories
- Leading position in high growth chronic therapies
- Specializes in technically complex products
- FY15 sales: US\$ 1,099 mn ⁽²⁾



Emerging Markets

- Presence in over 100 countries across Africa, Americas, Asia and Eastern & Central Europe
- Key focus markets – Brazil, Mexico, Russia, Romania, South Africa, and complementary & affiliated markets
- FY15 sales: US\$ 611 mn ⁽²⁾

Western Europe, Canada, ANZ & others

- Presence across majority of markets in Western Europe, Canada and ANZ
- Product portfolio includes differentiated offerings for hospitals, injectables and generics for retail market
- FY15 sales: US\$ 381 mn ⁽²⁾

Note:

(1) As of October, 31, 2015 using spot exchange rate of INR/USD = 65.22.

(2) Using average exchange rate for FY15 of INR/USD = 61.13

Includes Western Europe, Canada, Australia & New Zealand, Japan and other markets.

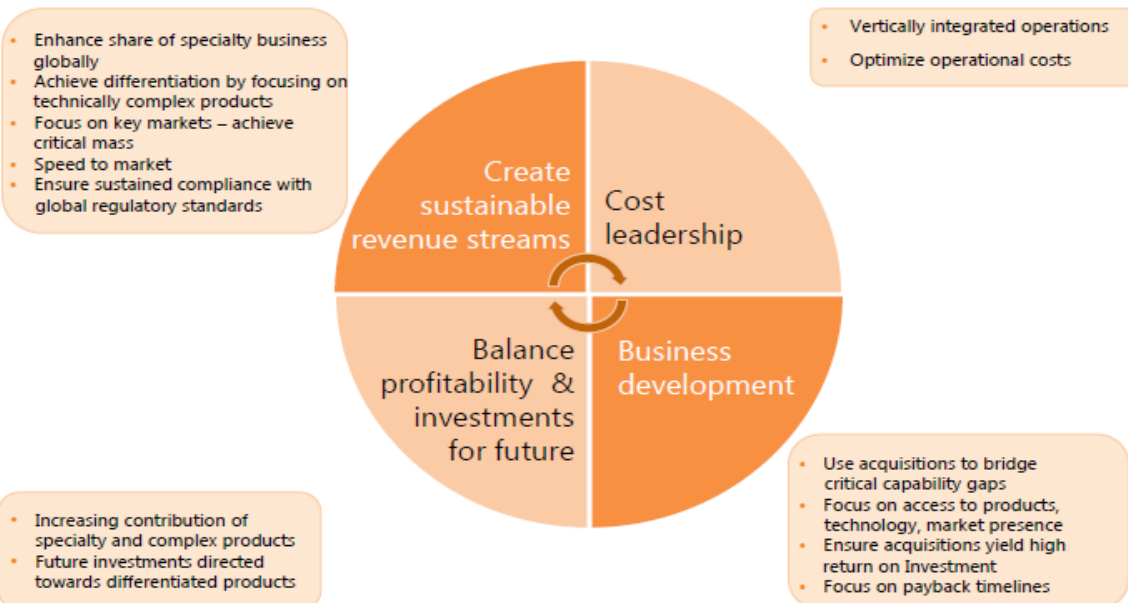
All sales numbers in US\$ for 12 months ended March 31, 2015.

* Source: Evaluate Pharma for 12 months ended Dec 2014

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Driving Long Term Growth



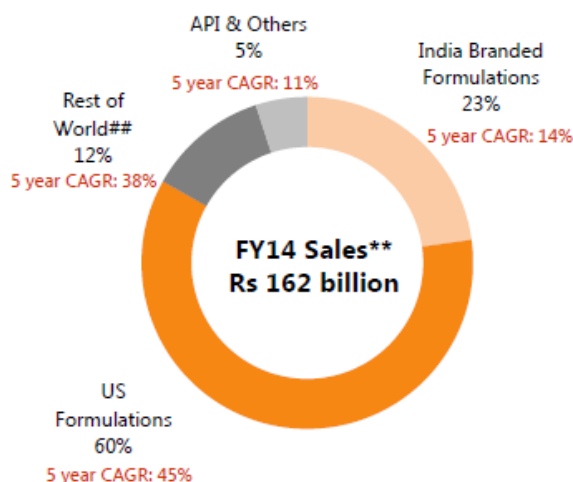
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Highly Diversified Revenue Base

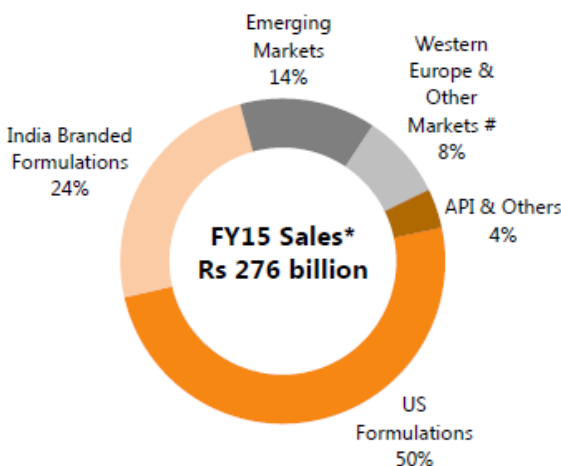


Sun Pharma (Pre Ranbaxy Acquisition)



** Sales for Sun Pharma (excluding Ranbaxy) for 12 months ended Mar' 14.
Includes all formulations sales excluding US and India

Sun Pharma (Post Ranbaxy Acquisition)



* Sales for Sun Pharma (including Ranbaxy) for 12 months ended Mar' 15.
Includes Western Europe, Canada, Australia & New Zealand, Japan and other markets.

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Leadership in key therapeutic areas*

Number 1 Ranking with 13 Doctor Categories*



Ranking (Sun Pharma)

Specialist	Oct '14
Psychiatrists	1
Neurologists	1
Cardiologists	1
Orthopaedic	1
Ophthalmologists	1
Gastroenterologists	1
Nephrologists	1
Diabetologists	2
Consulting Physicians	5
Dermatologists	6
Urologists	6
Chest Physicians	5
Oncologists	8

Ranking (Sun + Ranbaxy)

Specialist	June '15
Psychiatrists	1
Neurologists	1
Cardiologists	1
Orthopaedic	1
Ophthalmologists	1
Gastroenterologists	1
Nephrologists	1
Diabetologists	1
Consulting Physicians	1
Dermatologists	1
Urologists	1
Chest Physicians	1
Oncologists	1

Improved
Rankings
due to
Ranbaxy
acquisition



*Ranks based on prescription share

Source-Strategic Marketing Solutions and Research Centre (SMSRC) Prescription Data

Introduction to Division of Sun Pharmaceutical in which Summer Internship project was done:



The Classic division of SUN Pharmaceuticals is Multi speciality division. It is second largest acute business unit in Sun Pharmaceuticals.

Brands in the Classic Business Unit are:

Sporidex

Silverex

Zanocin

Mobizox

Crixan

D-Well aq

Riflect

Calmpose

Dolamide

Caverta

1. Introduction to Musculoskeletal Disorder/Disease:

Musculoskeletal (MS) pain is responsible for poor quality of life and decreased productivity. The origin of most musculoskeletal disorders (MSDs) lies in a mismatch between the external load and the capacity of the human body to resist biomechanical and physiological strain. Excessive forces can trigger different Pathophysiological processes depending on the tissues affected. It is the magnitude, duration and frequency of loading as well as the time for recovery which determine the physiological effect. Different symptoms in different body sites will depend on how far the physiological processes have advanced. The capacity depends on individual factors such as body build and size, gender, age, and general health, and it weakens with age due to MSDs. However, loading is necessary in order to maintain the capacity and this can be enhanced by an appropriate dosing of the mechanical load.

Musculoskeletal pain is a known consequence of repetitive strain, overuse, and work-related musculoskeletal disorders. These injuries include a variety of disorders that cause pain in bones, joints, muscles, or surrounding structures. The pain can be acute or chronic, focal or diffuse. Low back pain is the most common example of chronic musculoskeletal pain. Other examples include tendonitis and tendinosis, neuropathies, myalgia and stress fractures.

Pathophysiology:

The pathophysiology of musculoskeletal pain is not completely clear, but inflammation, fibrosis, tissue degradation, neurotransmitters, and neurosensory disturbances have been implicated.

- **Inflammation:** Injury induces increased pro-inflammatory cytokines and mediators in affected tissues and systemically. This increase leads to peripheral nociceptor sensitization.
- **Fibrosis:** Inflammation can induce fibrotic scarring (i.e., increased collagen within and between cells and tissues), which reduces gliding of tissues during movement, leading to stretch injuries and more pain.
- **Tissue degradation:** Increased inflammatory mediators induce increases in matrix metalloproteinase's (enzymes that degrade extracellular matrices), lowering tissue load tolerance and leading to further injury and more pain.

- Neurotransmitters: Levels of substance P, calcitonin-related related peptide, and N-methyl-D-aspartate (NMDA) are elevated in tendons, dorsal root ganglia, and spinal cord dorsal horns.
- Neurosensory/neuroimmune factors: Hypersensitivity, with increased levels of neurotransmitters, inflammatory mediators and cytokines, causes peripheral nociceptor sensitization or central amplification of pain. Hyposensitivity occurs with nerve compression from fibrosis

MSDs can appear with various symptoms of discomfort like pain, fatigue, muscle weakness, stiffness and limitation of movements, sensory loss and numbness, or local swelling and increased heat due to inflammation. Different body structures (muscles, tendons, joints, bones, nerves) tend to have different pathophysiological mechanisms behind the symptoms.

One common feature for most MSDs is the mismatch between the external load due to physical exertion and posture and the capacity of the human body to withstand that load. In addition to the magnitude of load, the duration and frequency of loading and recovery periods are important. The capacity to resist a load will vary according to individual characteristics (body build and size, gender, age, general health). The capacity varies with time and the human body adapts to the loading (e.g. training effects/ weakening).

Clinical Features:

- The pain can be acute or chronic, focal or diffuse in musculoskeletal or associated neural tissues.
- Clinical symptoms include:
 - 1) local symptoms of pain or widespread and persistent pain
 - 2) tenderness
 - 3) peripheral nerve irritation
 - 4) weakness
- Symptoms progressively increase with greater tissue injury and inflammation, with an increase in affected anatomical sites, i.e., increased tender points.
- Symptoms are exacerbated by work-related or personal stress, for example, poor control over one's work, difficult relationships, and time pressure.
- Nerve conduction velocity decreases in an involved peripheral nerve.

- Symptoms have diurnal fluctuation. At first, symptoms subside with cessation of work (i.e., between shifts, over weekends, and during vacations). As exposure persists and tissue injury progresses, symptoms may be insufficiently alleviated by rest, and constant pain may develop.
- Musculoskeletal disorders symptoms:

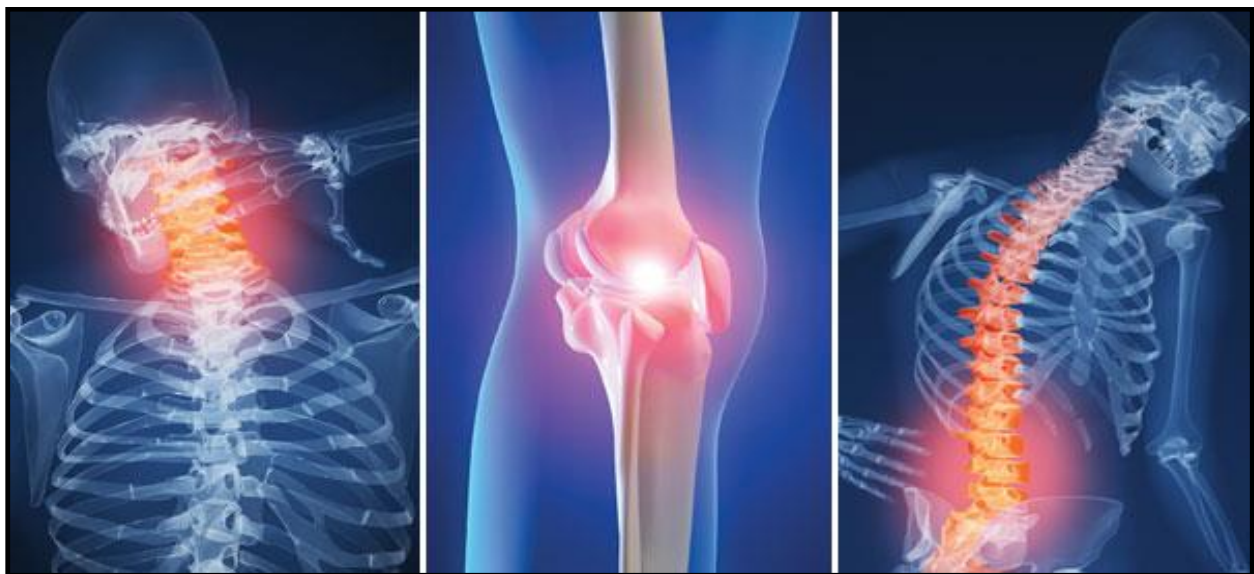
Pain in lower back
Pain in lower legs
Pain in hip buttock

Pain in Upper back
Pain in shoulders
Pain in thighs

Pain in limbs
Pain in neck

Pain in Knees
Pain in forearm

Pain in Joints
Pain in ankle



What is Pain?

Pain is an unpleasant sensation that serves as a warning signal to let you know something is not right with your body. Pain is controlled by the nervous system and is very a complex process. It occurs when an external stimuli, for example, touching a hot pan, triggers receptor nerve cells to send messages through your spiral cord to your brain. These receptors can sense heat, cold, light, touch, pressure, and pain. Pain can occur in many different areas of your body and range from mild discomfort to unbearable.

Origins of pain

Pain can occur in many different areas of your body, for example head, back, muscles, joints, and many more. Not only are the areas of pain varied, the manner in which pain is felt varies from one individual to another. Different people can assess the same pain anywhere from mild to “unbearable”. There is, however, agreement on one point: most people who suffer from pain want it to disappear as quickly as possible.

Chronic Pain:

Pain that is persistent and ongoing or keeps returning is classified as chronic and usually lasts longer than 6 months. Pain becomes chronic when the nervous system is overloaded by continuous pain stimulus. The nervous system fights back against this ongoing pain signal with complex changes, and as a result pain sensors can become much more sensitive. Meanwhile, the pain-inhibiting signals from the brain become weaker.

Over time, the pain may disconnect from its source and may persist even after the original injury has healed. Prompt and effective treatment can prevent acute pain from becoming chronic. Identify your pain to understand the best treatment to get you moving again.

Unfortunately pain is essential

Pain has a vitally important function: it serves as the body’s warning signal. Pain occurs when physical, temperature, chemical, or electrical stimuli exceed a certain threshold, for examples when you touch a hot pan. It signals when damage to the

body is occurring. Such damage can cause swelling, also referred to as inflammation, which in turn causes pain.

How the body detects pain

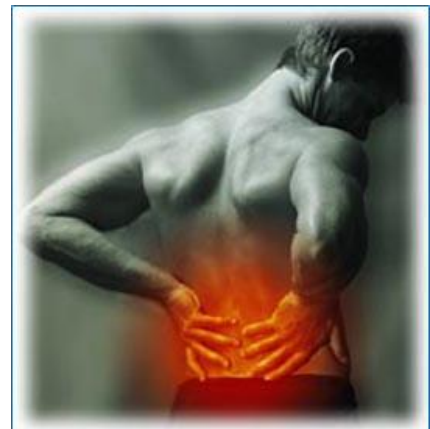
When you touch something hot or cut yourself, chemical messages are released which activate pain sensors, called sensory nerves, in your skin. These nerves then pass the pain message to your brain via the spinal cord, which is itself a bundle of nerves. The spinal cord links your brain to all parts of the body and is constantly sending and receiving information. Your brain will then perceive the pain and send messages back to the damaged area sometimes before you know it. For example, if you burn yourself on a hot stove, your brain will reflexively pull your hand back before the pain is consciously perceived.

Identify your pain type:

Back pain:

Most people will be affected by back pain at some point in their lives. Most frequently, the area affected is the lower back; with 80% of people affected at some point in their lives. The lower back refers to the area between the bottom of the ribs and the top of the legs.

Symptoms: Symptoms of back pain include soreness and stiffness. Tension felt in the neck, shoulders, buttocks and thighs can also be a sign of back pain.



Causes: Back pain develops for many different reasons. It can be triggered by everyday activities at home and at work. It can occur all of a sudden when you twist your back awkwardly, or it may develop gradually over time as a result of sitting or standing badly.

In general, cases of back pain are not associated with serious disease. It often resolves within 12 weeks.

Back pain causes include:

- bending awkwardly
- lifting, carrying, pushing or pulling incorrectly
- slouching in chairs

- standing or bending down for long periods
- twisting
- over-stretching
- driving in a hunched position
- driving for long periods without taking a break
- overuse of the muscles, usually due to sport or repetitive movements (repetitive strain injury)

For back pain lasting more than 6 weeks, please consult your doctor.

Neck & Shoulder Pain:

Neck pain, or a stiff neck, and shoulder pain are common complaints. Often tension is experienced in both areas at the same time.

Neck Pain: This includes conditions such as neck strain, neck sprain, whiplash, and other neck disorders.

Causes: Neck pain or a stiff neck often occurs as a result of bending your neck into an abnormal position, for example, by sleeping on too many pillows. Other causes include poor posture or from sitting in a draught for too long. As neck pain often occurs as a result from everyday activities, an obvious cause is often difficult to detect and so the pain is often referred to as ‘non-specific’ by doctors.



Symptoms: Neck pain occurs when the neck suddenly feels tight, it becomes uncomfortable or tension in the neck is felt when the head is turned up and down or even to the sides. Neck pain or stiffness usually gets better after a few days and is not a sign of any neck problem or serious underlying condition. If the pain or stiffness does not seem to be getting better after a few days and you are worried, or if you cannot control the pain with ordinary painkillers, consult your doctor.

Shoulder pain:

Shoulder pain is a symptom rather than a condition in itself. Shoulder pain can be a long-term problem, with up to half of people still having symptoms after 18 months.

Causes: Shoulder pain can be caused by a number of different shoulder disorders:

Frozen shoulder – a painful condition where joints become stiff, reducing normal movement in the joints or even preventing movement in the shoulder altogether

Rotator cuff disorders – the rotator cuff is a group of muscles and tendons that surround the shoulder joint and help to keep it stable



Shoulder instability

– Where the shoulder is unstable and has an unusually large range of movement (hypermobility)

Acromioclavicular joint disorders:

- Conditions that affect the joint at the very top of the shoulder. Frozen shoulder and rotator cuff disorder mostly affect middle-aged and older people, whilst shoulder instability and acromioclavicular joint disorders tend to affect younger people. This includes those who play sports that involve shoulder movements, such as bowling, tennis, or throwing, as well as such as rugby where your shoulder is exposed to a lot of pressure from contact with others or when you fall on your shoulder. If you are experiencing ongoing neck or shoulder pain, please consult your doctor.

Joint Pain/Osteoarthritis:

Joint pain can affect many different areas of the body such as fingers, wrist, toes or knee and it tends to show through stiffness, tenderness and swelling. Joint pain or arthritis involves inflammation of one or more joints and occurs in many different forms. There are a number of different types of arthritis that can result in a wide range of symptoms. Osteoarthritis tends to affect the knees, hands and hips, but may also affect the back, feet and neck. In osteoarthritis, the ability of the cartilage - the protective layer that covers the bone - to repair itself is reduced, resulting in a gradual loss of cartilage over time. The exposed bones can then rub together



causing swelling, also referred to as inflammation, pain and bony outgrowths into the joint, making the joint stiff and difficult to move.

Causes: As part of activity and movements in everyday life, joints are constantly dealing with pressure and damage. Your body is usually able to repair these damages by itself. Normally, this repair process will happen automatically without you noticing or seeing any symptoms. However, sometimes your body cannot repair the damage in and around the joints. This is referred to as osteoarthritis. The condition can present as ligament or tendon problems, inflammation in the joint itself and damage to the protective cartilage that allows your joints to move smoothly. There are various factors that cause the repair process to break down and increase the likelihood of osteoarthritis. These include: the joints previously being damaged through an injury or operation or other conditions such as rheumatoid arthritis (caused by the body's immune system), a genetic predisposition for the condition in family and obesity with joints being exposed to excess pressure.

Symptoms: Your joints may become knobby around the area of your bones forming bony lumps called osteophytes. As your bones thicken and broaden, your joints will become stiff, painful and difficult to move. There may also be a build-up of fluid in your joints because of the inflammation, which can cause them to swell up. Initial symptoms therefore often include swelling, pain around the joints and discomfort when moving. The level of joint pain can vary from infrequent to intense and can be very hard to manage.

Injuries - sprains, strains and bruises:

If you do sports or other physically challenging activities, you are likely to experience some form of injury at some point.

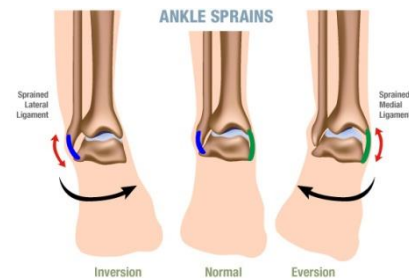
These injuries mostly affect your soft tissues, including muscles, ligaments and tendons that may be injured as a result of excessive forces like overstretching or sustaining a direct blow.

When tissues are injured, they go through a healing process. It starts with an inflammatory response that is vital for the tissues to heal well. During the inflammatory phase of healing, injured tissue is removed and it begins to be replaced. The injured area is very sensitive to further injuries because the new tissue is very delicate. So it is important that you give them time to heal. As the



healing process evolves, the area gradually becomes more resilient and normal function begins to return. If any injury does not show signs of improving after a few days, please consult your doctor or chartered physiotherapist to get properly assessed and make sure there is no fracture or bone injury.

Because sport is often the cause of injuries, here are some of the most common sports-related injuries.



Causes:

A strain occurs when a muscle is overstretched. Whilst a sprain is the forcible wrenching or twisting of a joint with partial or complete rupture of its muscles, but without dislocation. Traditionally a sprain is considered to be more serious than a strain. However, strains can lead to muscle tears as well.

Ankle sprains: Ankle sprains are common and can take weeks or even months to heal. Symptoms include a swollen and tender ankle. It is important to be aware that injuries to ligaments may cause ankle instability that could lead to foot problems, including osteoarthritis, in later life.

Groin strains: Common in football players, these injuries cause pain in the groin. The hip is fully mobile but there is extreme tenderness in the muscle tendons around the groin. Occasionally pain in this area can be caused by a hernia or it can be pain from an injury elsewhere like the back or the hip.

Bruises: Bruises, also known as contusions, usually develop after a bump or fall. Small blood vessels rupture or tear under the skin. This causes blood to leak into the tissues under the skin resulting in a blue/black colour. Bruises usually heal within 2 weeks, although bruises on the leg usually take longer to heal than those on the face or arms. If the bruise is still there after 2 weeks consult your doctor. As said, most bruises will go away on their own. However, severe bruising, pain and swelling that begins within 30 minutes of an injury may indicate a more serious problem, such as a fracture or severe sprain, and may require evaluation by a doctor.

Diagnosis and Treatment:

Diagnoses include peripheral neuropathies; lateral or medial epicondylitis/tendonitis; rotator cuff, bicipital, or wrist tendonitis; wrist sprain or strain; Achilles tendonitis; myositis and myalgia; osteoarthritis; cervical strain; and lower back pain. Management is typically multimodal:

- Physical therapy, primarily with an exercise program (aerobic, strengthening, stretching), together with physical modalities, such as heat or ice
- Splinting and/or orthoses
- Use of nonsteroidal anti-inflammatory drugs (NSAIDs), e.g., **Diclofenac**
- Reduction in workload or increased rest
- Stress management/behavioral intervention



1.1. Epidemiology of Musculoskeletal Disorders India:

Musculoskeletal Disorders are one of the major causes of morbidity, have a substantial influence on health and quality of life and impose an enormous burden of cost on healthcare system. The existing knowledge of musculoskeletal conditions comprises over 150 diseases and syndromes usually associated pain. They can broadly be categorized as joint diseases, spinal disorders and conditions resulting from Trauma. The burden of musculoskeletal disorders is global and looking at the gravity of the situation WHO declared 2000-2010 as the Bone and Joint decade. ⁽¹⁾ (Organization, WHO,2003)

Review on the existing literature on MSD shows that the incidence and prevalence of MSD varies with the change in the climatic conditions and geographic region. It also identifies the advancing age and female sex associated with increased incidence of MSD pain. One of the earliest COPCORD study on MSD in India was carried in Village Bhigwan under the aegis of ILAR/APLAR. The incidence of MSD as per the study was 12.8% among screened villagers (Chopra A, 1997).

A recent study of Rheumatic Musculoskeletal disorders conducted in the Urban Region of Pune, India, using the COPCORD Bhigwan Model, found 14.1% prevalence of MSD (A, 2009).

ICMR MSD in India report (conclusion): The three selected MSD's in study i.e Osteoarthritis, Rheumatoid Arthritis and Spinal cord disorders constituted major share of burden of musculoskeletal disorders. The prevalence of RA in Delhi was 0.17%, 0.19% in Dibrugarh and 0.62% in Jodhpur covering the sample from North, East and West India. The prevalence of OA in Delhi was 3.28% , it was found that to be 5.81% in Dibrugarh and 6.52% in Jodhpur. Spinal cord disorders prevalence was Delhi 4.8%, Jodhpur 5.42% and in Dibrugarh 5.76%.

The high prevalence rate of MSD's in country itself demands increased care for musculoskeletal disorders. Therefore there is a need of targeted approach and preventive treatment with the medications to prevent the tertiary care conditions.

1.2. Treatment of Musculoskeletal Disorders:

Management of Mild-to-Moderate Pain

A wide variety of treatment options are available to manage musculoskeletal pain. Evidence based approaches include non-pharmacological and pharmacological interventions. Generally, treatment is tailored to fit the needs and risk factors of the individual. Care for patients with chronic pain can involve a multidisciplinary team that includes primary care physicians, medical specialists, psychiatrists, psychologists, physical therapists, occupational therapists, social workers, pharmacists, relaxation therapists, vocational counselors, and nurses.

Non-pharmacological Treatment:

Multiple non-pharmacological therapies are available for the management of musculoskeletal pain disorders. These measures can be divided into physical and psychosocial modalities. Physical measures include bed rest; exercise; local heat or cold therapy; manual therapies (spinal manipulation, massage, and mobilization techniques); and stimulation techniques (acupuncture, transcutaneous electrical nerve stimulation [TENS], and percutaneous electrical nerve stimulation). Psychosocial interventions include patient education, relaxation techniques, biofeedback, guided imagery, support groups, family counseling, and psychotherapy. Practices such as tai chi—which includes specialized movements and breathing techniques, combining both physical and psychosocial measures—have been shown to improve functional ability, reduce pain, and improve psychosocial health in patients with musculoskeletal conditions.

Dietary supplements may be an alternative treatment for patients wary of prescription medications. Glucosamine and chondroitin, methylsulfonylmethane (MSM), and omega-3 fatty acids have been shown to reduce pain and improve physical function in patients with musculoskeletal-related conditions such as osteoarthritis and low back pain (James W. Atchison & Christopher M. Herndon, 2013).

Pharmacological Treatment:

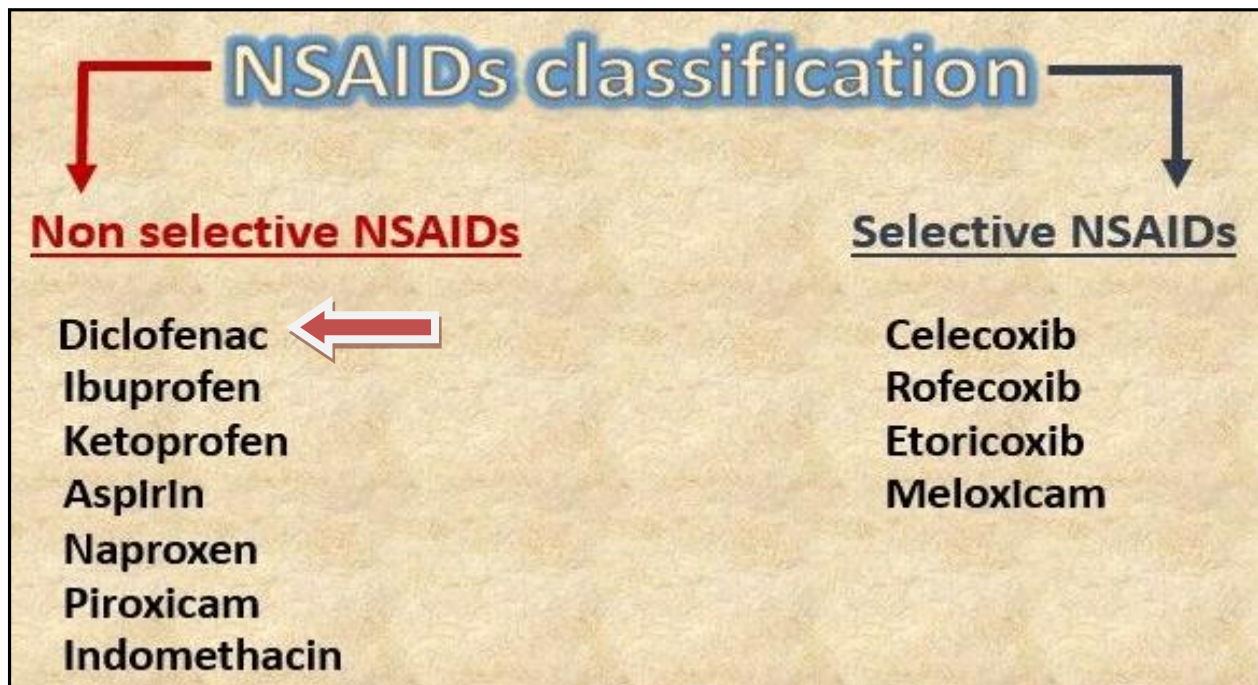
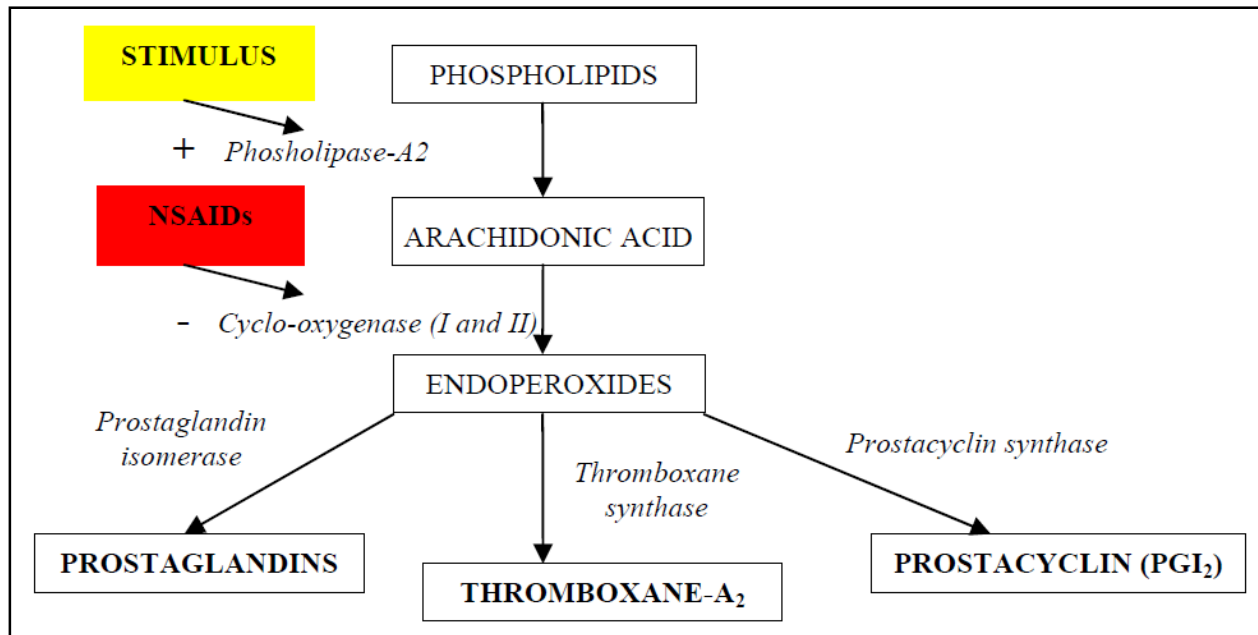
A variety of oral and topical analgesic medications are available for the treatment of musculoskeletal disorders and injuries. Analgesics include opioids, nonopioids, and adjuvant analgesics. They are available in many forms, both over-the-counter (OTC) or by prescription. Nonopioid analgesics include acetaminophen, salicylates, and NSAIDs. Adjuvant analgesics (or coanalgesics) are drugs with primary indications other than pain but have secondary effects of analgesia. They include muscle relaxants, anticonvulsants, antidepressants, corticosteroids, and alpha-2 adrenergic agonists. Duloxetine, a serotonin-norepinephrine reuptake inhibitor, recently received FDA approval for chronic musculoskeletal pain, based on studies in knee osteoarthritis and low back pain. (James W. Atchison & Christopher M. Herndon, 2013).

Evidence based treatment practices involving NSAID's:

NSAIDs are among the most commonly used medications for musculoskeletal conditions because of their known effectiveness as anti-inflammatory and analgesic agents. A recent study in The Journal of Pain found that NSAIDs were the most preferred and prescribed drugs for chronic pain. In 2012, 98 million prescriptions were filled for NSAIDs, and approximately 23 million people in the United States used OTC NSAIDs regularly. Ibuprofen is the most commonly used NSAID in the United States, while Diclofenac is the most popular throughout the world. NSAIDs have anti-inflammatory, analgesic, and antipyretic properties. They are indicated for the treatment of mild-to-moderate pain in various acute and chronic inflammatory conditions. Their efficacy has been established in numerous acute and chronic pain conditions including osteoarthritis, rheumatoid arthritis, low back pain, neck pain, headache, dysmenorrhea, and gout. NSAIDs are generally preferred over opioids because of their established effectiveness and limited potential for abuse. NSAIDs comprise traditional NSAIDs and cyclooxygenase-2 (COX-2) inhibitors (or coxibs). All NSAIDs inhibit the production of prostaglandins by inhibiting the activity of PGG/H synthase, also known as cyclooxygenase (COX). COX exists in 2 isoforms (COX-1 and COX-2), which differ in tissue expression and regulation. The therapeutic effects of NSAIDs are attributed to inhibition of COX-2 in inflammatory sites. Specificity to the COX isoform is a key factor that influences both efficacy and safety. NSAIDs are

available both OTC and by prescription and in oral and topical formulations. Nonprescription aspirin, ibuprofen, and naproxen are sold at low doses and can be found in combination products used for pain and fever or cough and cold. Many oral formulations are available as generic drugs. In 2007, a topical Diclofenac patch was approved for the treatment of pain. Diclofenac is the first and only NSAID approved for topical use. Currently, 3 topical formulations, all salts of Diclofenac, are commercially available in the United States for use in pain: 1.3% Diclofenac epolamine transdermal patch, 1% Diclofenac sodium gel, and Diclofenac sodium 1.5% topical solution. The transdermal patch is approved for acute musculoskeletal injury (minor sprains, strains, and contusions), and the solution and gel are approved for the treatment of osteoarthritis pain. Topical NSAIDs were developed as an alternative to oral NSAIDs and may be beneficial for localized pain. A meta-analysis evaluating 34 studies from 7,688 adults with chronic musculoskeletal pain found that topical NSAIDs provided adequate pain relief, equivalent to oral NSAIDs for hand and knee osteoarthritis. Currently, there is a lack of sufficient evidence comparing oral and topical NSAIDs for other chronic pain conditions. Systemic absorption is lower with topical agents; thus, they are associated with fewer adverse events. The incidence of local adverse events, however, is increased with topical NSAIDs. In the past 5 years, various updated guidelines have included recommendations for the use of topical NSAIDs, particularly in patients considered at gastrointestinal or cardiovascular high risk (Surgeon, 2013) (Hochberg MC, 2012) (Panel, 2009).

Mechanism of Action of NSAID's:

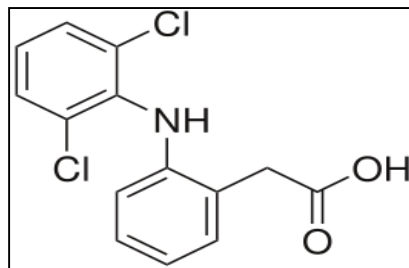


Diclofenac as NSAID's:

Diclofenac is a non steroidal anti-inflammatory drug (NSAID) taken or applied to reduce inflammation and as an analgesic reducing pain in certain conditions.

The name "Diclofenac" derives from its chemical name: 2-(2,6-dichloranilino) phenylacetic acid.

Diclofenac was first synthesized by Alfred Sallmann and Rudolf Pfister and introduced as Voltaren by Ciba-Geigy (now Novartis) in 1973 (Roy Altman, 2015).



In the United Kingdom, United States, India, and Brazil Diclofenac may be supplied as either the sodium or potassium salt; in China, it is most often supplied as the sodium salt, while in some other countries it is only available as the potassium salt. Diclofenac is available as a generic drug in a number of formulations, including Diclofenac diethyl amine, which is applied topically. Over-the-counter (OTC) use is approved in some countries for minor aches and pains and fever associated with common infections. As of 2015 the cost for a typical month of medication in the United States is 50 to 100 USD (al, 2015).

Formulations of Diclofenac:

Forms of Diclofenac:

Diclofenac exists in two forms - the sodium salt (diclofenac sodium) and the potassium salt (diclofenac potassium). Each has the same amount of diclofenac base - the main difference is that diclofenac potassium is slightly more soluble in water than diclofenac sodium. Diclofenac potassium is generally considered to be more quickly absorbed and have a faster onset of analgesic activity than diclofenac sodium.

Pennsaid is a minimally systemic prescription topical lotion formulation of 1.5% w/w diclofenac sodium, which is approved in the US, Canada and other countries for osteoarthritis of the knee.

Flector Patch, a minimally systemic topical patch formulation of diclofenac, is indicated for acute pain due to minor sprains, strains, and contusions. The patch

has been approved in many other countries outside the US under different brand names.

Voltaren and Voltarol contain the sodium salt of diclofenac. In the United Kingdom, Voltarol can be supplied with either the sodium salt or the potassium salt, while Cataflam, sold in some other countries, is the potassium salt only. However, Voltarol Emulgel contains diclofenac diethyl ammonium, in which a 1.16% concentration is equivalent to a 1% concentration of the sodium salt. Diclofenac is available in stomach acid-resistant formulations (25 and 50 mg), fast-disintegrating oral formulations (25 and 50 mg), powder for oral solution (50 mg), slow- and controlled-release forms (75, 100 or 150 mg), suppositories (50 and 100 mg), and injectable forms (50 and 75 mg).

Diclofenac is also available over-the-counter in some countries: 12.5 mg diclofenac as potassium salt in Switzerland (Voltaren dolo), the Netherlands (Voltaren K), and preparations containing 25 mg diclofenac as the potassium salt in Germany (various trade names), New Zealand, Australia, Japan, (Voltaren Rapid), and Sweden (Voltaren T and Diclofenac T). Diclofenac as potassium salt can be found throughout the Middle East in 25-mg and 50-mg doses (Cataflam). Solaraze (3% diclofenac sodium gel) is topically applied, twice a day for three months, to manage the skin condition known as actinic or solar keratosis. Parazone-DP is combination of diclofenac potassium and paracetamol, manufactured and supplied by Ozone Pharmaceuticals and Chemicals, Gujarat, India.

On 14 January 2015, diclofenac oral preparations were reclassified as prescription-only medicines in the UK (<http://www.drugs.com/international/diclofenac.html>). (<https://www.gov.uk/drug-device-alerts/drug-alert-oral-diclofenac-presentations-with-legal-status-p-reclassified-to-pom>). The topical preparations are still available without prescription. Diclofenac formulations are available worldwide under many different trade names. *The Topical formulation for management of Pain has been found to have considerable advantages over the Oral formulation in treating MSD's*



4 *benefits of*
TOPICAL PAIN RELIEF
— compared to —
ORAL MEDICATIONS

Localized treatment	Speed of effect
Lesser systemic side effects	Compounding (Customized dose)

Topical Analgesics:

Topical analgesics, formulated as creams, gels, and patches are applied locally to the skin and influence pain signaling by local actions on sensory nerve endings and adjacent tissue following dermal penetration. Topical analgesics are widely available without prescription, and widely advertised. Consumers need to have the best information available, as well. The evidence is that topical NSAIDs are effective and safe (Healthcare, March,2005). Bandolier reviews were sought for topical capsaicin, rubefacients, and NSAIDs, in acute and chronic painful conditions.

Topical Capsaicin:

Capsaicin studies were conducted in chronic neuropathic and musculoskeletal pain, at different strengths of cream in trials of eight weeks duration. In neuropathic conditions in six trials (656 patients), topical capsaicin (0.075%) was better than placebo with an NNT of 5.7 (95% CI 4.0 to 10). In musculoskeletal conditions in three trials (368 patients) topical capsaicin (0.025% or plaster) was better than

placebo with an NNT of 8.1 (4.6 to 34). About one third of patients experienced local adverse events with capsaicin, who would not have done so with placebo.

Topical Rubefacients:

Rubefacient studies consisted entirely of topical salicylates in trials using one week outcomes for acute conditions and two week outcomes for chronic conditions. In acute conditions in three trials with 182 patients topical salicylate was significantly better than placebo with an NNT of 2.1 (1.7 to 2.8). In chronic conditions in six trials with 429 patients topical salicylate was significantly better than placebo with an NNT of 5.3 (CI 3.6 to 10.2), but the three larger, more valid studies were without significant effect. Local adverse events and withdrawals were generally rare in trials that reported them.

<u>Some important Topical Rubefacients</u>	<u>Uses</u>
Glucosamine sulphate	Given in the treatment of rheumatic disorders
Camphor	Applied externally, camphor acts as a rubefacient and mild analgesic
Methyl salicylate	Salicylic acid derivative irritant to the skin and is used in rubefacient preparations
Menthol	Vasodilation causing sensation of coldness followed by analgesic effect
Dimethylsulphoxide	(DMSO) exceptional solvent properties. Anti-inflammatory & vasodilatory properties
Heparin	Anticoagulant and found in topical preps for various inflammatory disorders

1.3. Topical NSAID'S & Formulation:

Topical NSAIDs were well investigated in acute painful conditions, which were all musculoskeletal in nature, in trials using one week outcomes. Topical NSAID was significantly better than placebo in 19 of the 26 trials, with a pooled relative benefit of 1.6 (1.4 to 1.7), and NNT of 3.8 (3.4 to 4.4) compared with placebo for the outcome of half pain relief at seven days. Topical NSAIDs were well investigated in chronic painful conditions, which were all musculoskeletal in nature, in trials using two week outcomes. Topical NSAIDs were clearly better than placebo in chronic musculoskeletal pain, with an NNT of 4.4 (3.6 to 5.6) in the best trials. Studies were generally of short duration, and no single preparation could be shown to be better than another. No study showed oral NSAID to be better than topical NSAID. Local adverse events, systemic adverse events, or withdrawals due to an adverse event were rare, and no different between topical NSAID and placebo (Healthcare, March,2005).

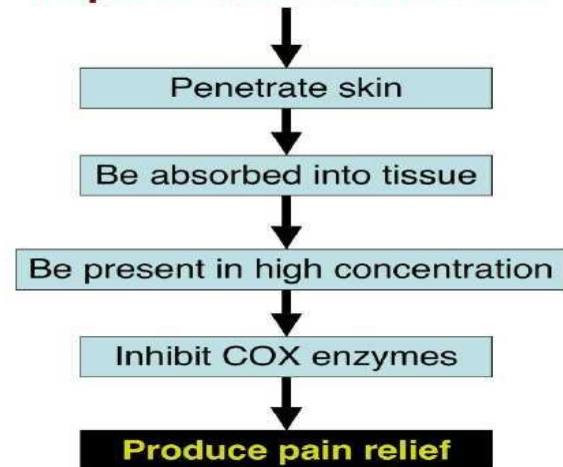
Topical NSAID's and other Topical Analgesics are available in various forms and formulations:

<i>Gel</i>	<i>Liquid</i>
<i>Cream</i>	<i>Patches</i>
<i>Ointment</i>	<i>Injections</i>
<i>Spray</i>	<i>Aerosols etc</i>

Topical Analgesic Cream: Creams are a semi-solid emulsion, half oil and half water. This formulation is typically the easiest to use and is preferable by most patients. They spread easily, absorb quickly and wash



Topical NSAID has to:



off with water. They have a medium viscosity or heaviness, and are reasonably hydrating without feeling too heavy on your skin. Creams are always packaged in a tub or a tube; they are too thick to be dispensed in a pump. Creams are often used to treat acne in patients whose skin is somewhat dry, as the creams promote hydration. Creams are also more beneficial in darker skin, which in general is more easily irritated than lighter skin. The cream used to treat pain is Topical Analgesic cream.

Topical Analgesic Ointment: Ointments which are used to treat Analgesia. Ointments are 80% oil and 20% water. These products feel greasy, do not absorb well and are generally not easy to use on large areas. They are ‘occlusive,’ which means they

trap moisture and heat in very well. Ointments promote medication absorption over all other formulations. If an ingredient is in an ointment, it is always more potent than the exact same ingredient packaged in a cream or lotion. For example, amcinonide is a topical steroid. In an ointment it is considered high potency, and in a cream or lotion it is considered medium-high potency.



Topical Analgesic Spray:

A Spray is fine jet of liquid discharged from a pressurized container. A spray intended for topical administration to relieve pain and Inflammation.



The choice of delivery system for topical acne medications depends upon your skin type (oily versus dry) and preference. Gels are drying; they may be appropriate for individuals with oily skin. Creams and lotions tend to be moisturizing. Foams are easy to apply to hair-bearing areas (<http://bellevueacneclinic.com/what-is-the-difference-between-cream-ointment-and-lotion.html>).

Topical Analgesic Gel:

A gel is a solid or semisolid system of at least two constituents, consisting of a condensed mass enclosing and interpenetrated by a liquid. Topical



Analgesic Gels are used to relieve pain & inflammation and is applied topically.

Advantages of Gel:

- Gels are used to achieve optimal cutaneous and percutaneous drug delivery.
- They can avoid gastrointestinal drug absorption difficulties caused by gastrointestinal pH.
- Gels are having property to avoid enzymatic activity and drug interaction with food and drinks.
- They can substitute for oral administration of medication when the route is unsuitable.
- They can avoid the first pass effect, that is, the initial pass of drug substance through the human body.
- They avoid systemic and portal circulation following gastrointestinal absorption.
- Gels are not deactivated by liver enzymes because the liver is bypassed.
- They are non-invasive and have patient compliance.
- They are applied over skin for slow and prolonged absorption.
- Gels have also been applied in pharmacy to some viscous suspension for oral use for example Aluminum hydroxide gel.
- They have localized effect with minimum side effects.

Delivery through skin:

Delivery of drugs to the skin is an effective and targeted therapy for local dermatological disorders. Topical gel formulations provide a suitable delivery system for drugs because they are less greasy and can be easily removed from the skin

Advantages of This Route:

- It provides a largest surface area.
- It avoids first-pass effects, gastrointestinal irritation.
- It avoids metabolic degradation associated with oral administration.

Mechanism of Drug Absorption:

The principal mechanisms of drug absorption are:

1. Passive diffusion
2. Pore transport
3. Facilitated diffusion
4. Active transport
5. Ionic or electrochemical diffusion
6. Ion-pair transport
7. Endocytosis

Physiological Factors Affecting Skin Penetration:

1. Skin integrity
2. Skin Hydration
3. Skin temperature
4. Regional variation
5. Traumatic/pathologic injury to skin
6. Cutaneous drug metabolism

Formulation Factors Affecting Skin Penetration:

1. Penetration enhancer.
2. Occlusivity
3. Drug concentration
4. pH
5. Solubility
6. Surfactant

Classification of Gels is Following:

- A. Controlled release gels
- B. Organogels
- C. Extended release gels
- D. Amphiphilic gels
- E. Hydrophilic gels
- F. Non aqueous gels
- G. Bioadhesive gels
- H. Thermo sensitive sol-gel reversible hydro gels

- I. Complexation gels
- J. Hydro gel

Topical Analgesic Advantages & Disadvantages:

Advantages	Disadvantages
Production of low plasma drug levels and decreased systemic adverse events	Needs appropriate physicochemical properties (molecular size, aqueous/lipid solubility) for dermal and tissue penetration
Avoidance of factors that can limit oral bioavailability (first pass metabolism, influence of gastric factors on absorption)	Skin characteristics and disease states can alter the extent of dermal absorption
Convenience and increased adherence to therapy	Potential for local skin reactions (<i>e.g.</i> , rash, pruritus, dry skin, irritation)

2. Rationale for Study:

MSDs are an increasing healthcare issue globally, being the second leading cause of disability (Barbe, Gallagher, Massicotte, Tytell, Popoff, & Barr-Gillespie, 2013). Musculoskeletal conditions are the most common cause of severe long term pain and physical disability. The prevalence of musculoskeletal conditions increases markedly with age. Musculoskeletal conditions are the main cause of disability among older age groups. The pain and physical disability brought about by musculoskeletal conditions affect social functioning and mental health, further diminishing the patient's quality of life.

Topical analgesics are promising as a strategy for pain treatment, as they are associated with lower incidence of side effects (Flores MP1, 2012 Mar-Apr). Diclofenac molecule is widely used for NSAID for Topical Analgesic gel.

The strength of Diclofenac available in Topical Analgesic gel available in majority in India is 1% Diclofenac & Combination Gel. In man the percutaneous absorption was 6% of the dose of Emulgel Diclofenac 1% & In man, upon daily topical administration of 3 times 2.5 g cream formulation (10 mg/cm²) the diclofenac steady state plasma levels were 20 to 40 (Riess W, 1986 Jul;36(7):1092-6).

The above results shows that higher concentration of Diclofenac 2% in Gel formulation will be better to reduce the number of application and would be efficacious to reduce high intensity pain because of higher concentration as per the product “ Voltarol® 12 Hour Emulgel® P 2.32% Gel” marketed in U.K (MHRA approved product).

The rationale for the study is to find out the need and awareness of 2% Diclofenac and combination among doctors and to find out doctor's perception and preferences for recently available topical analgesic.

3. Market Research (Desk Research):

Research Objectives:

- To find out the market share of Topical Analgesic segment.
- To find out the trends and share of Topical Analgesic Gel market.
- To find out Leading Brands and Molecules in Topical Analgesic Gel market.
- To find out the prescription share and trends of specialties in Topical Analgesic Gel market.

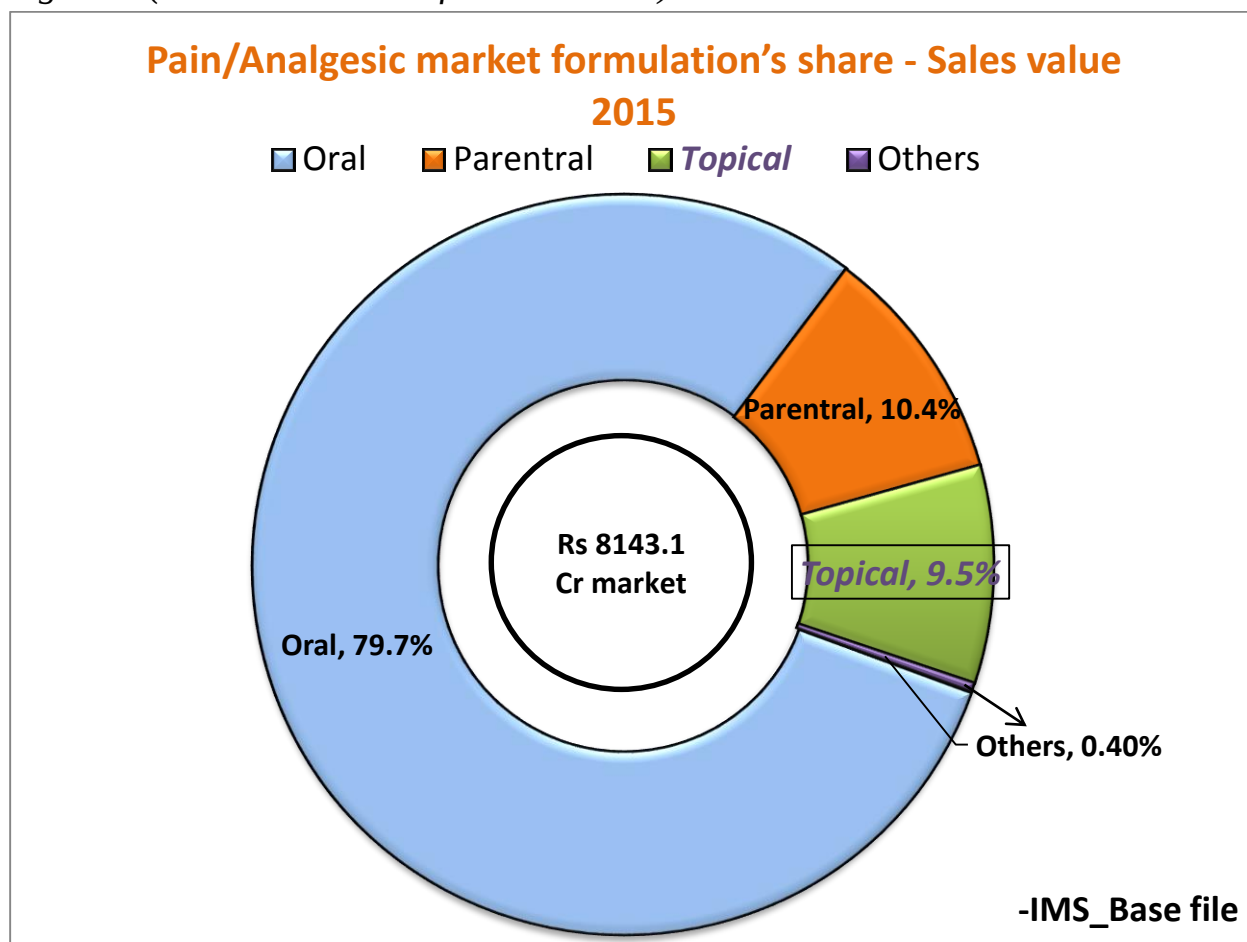
Research Methodology:

Parameters	Descriptions
Research Type	Descriptive research
Type of Data	Secondary data
Source of data	IMS_Base file (5years-2011-'15) and SMSRC Rx data (3 years- 2013-'15)
Profile of data	Topical Analgesic market & Prescriptions trends and share's
Analysis tool	MS Excel 2007
Analysis representation	Charts, Graphs and Tables

**ANALYSIS AND INTERPRETATION
OF SECONDARY DATA (IMS_BASE
FILE AND SMSRC R_x DATA) AS
PER OBJECTIVES DEFINED.**

Total Plain Analgesic Market and formulations share:

Figure: 1(Source: IMS Base file 2011-2016)

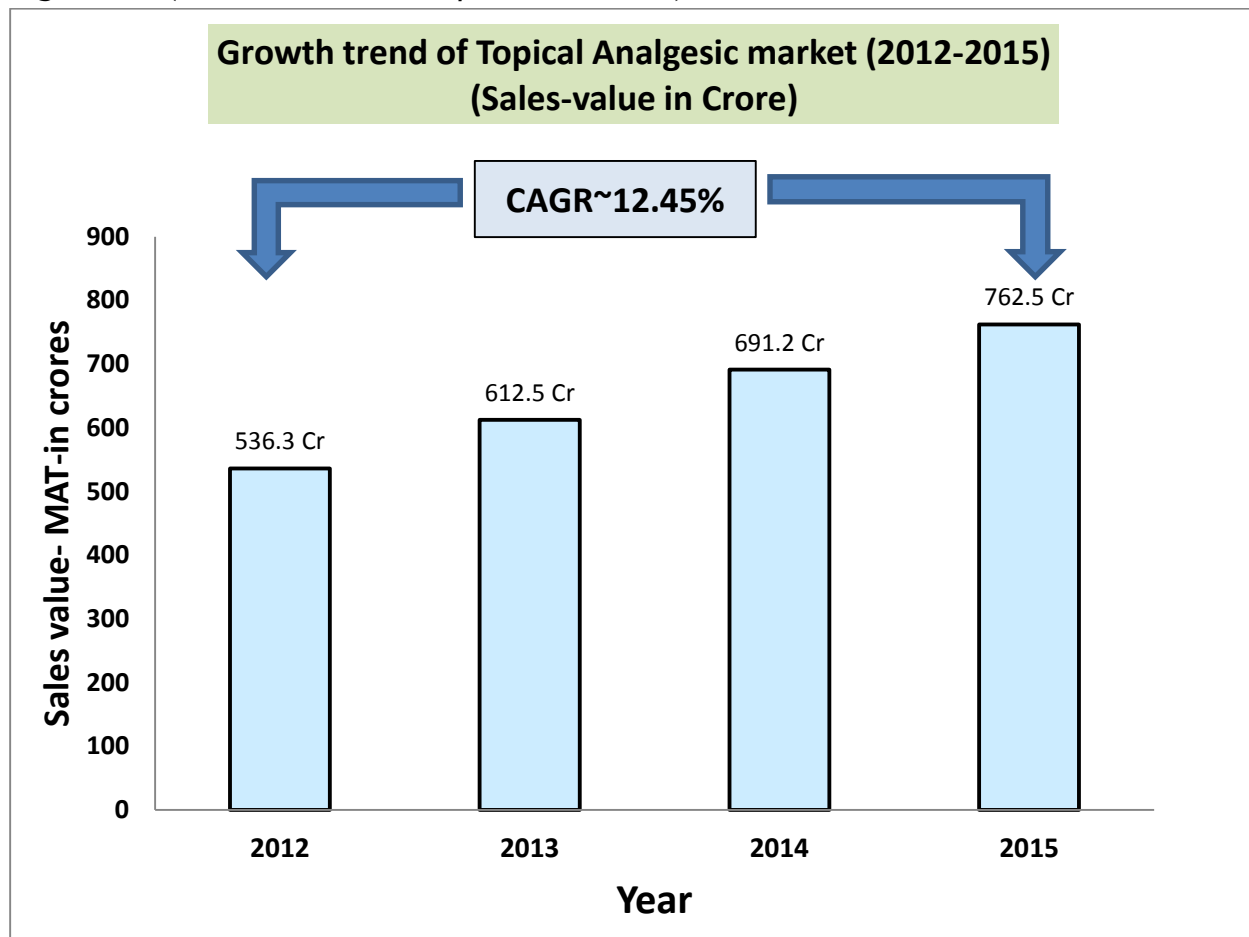


Interpretation:

In 2015, the total sales value of Pain/Analgesic drugs in Indian market is calculated to be Rs 8143.1 Cr (Source: IMS data). Out of that, the share of Oral formulation was 79.7% (Rs 6490.05 Cr), Parenteral - 10.4% (Rs 846.3 Cr), Topical – 9.5% (Rs 773.59 Cr) (Including Topical Patches) and others were 0.40% in Pain/Analgesic segment. This shows that Oral formulation has highest Sales value share as compared to other formulations. Though Topical Analgesic formulation is 9.5%, but in terms of its value of Rs 773.59 Cr, is a potential and big market.

Growth of Topical Analgesic segment in Indian market (2012-2015):

Figure: 2. (Source: IMS Base file 2011-2016)

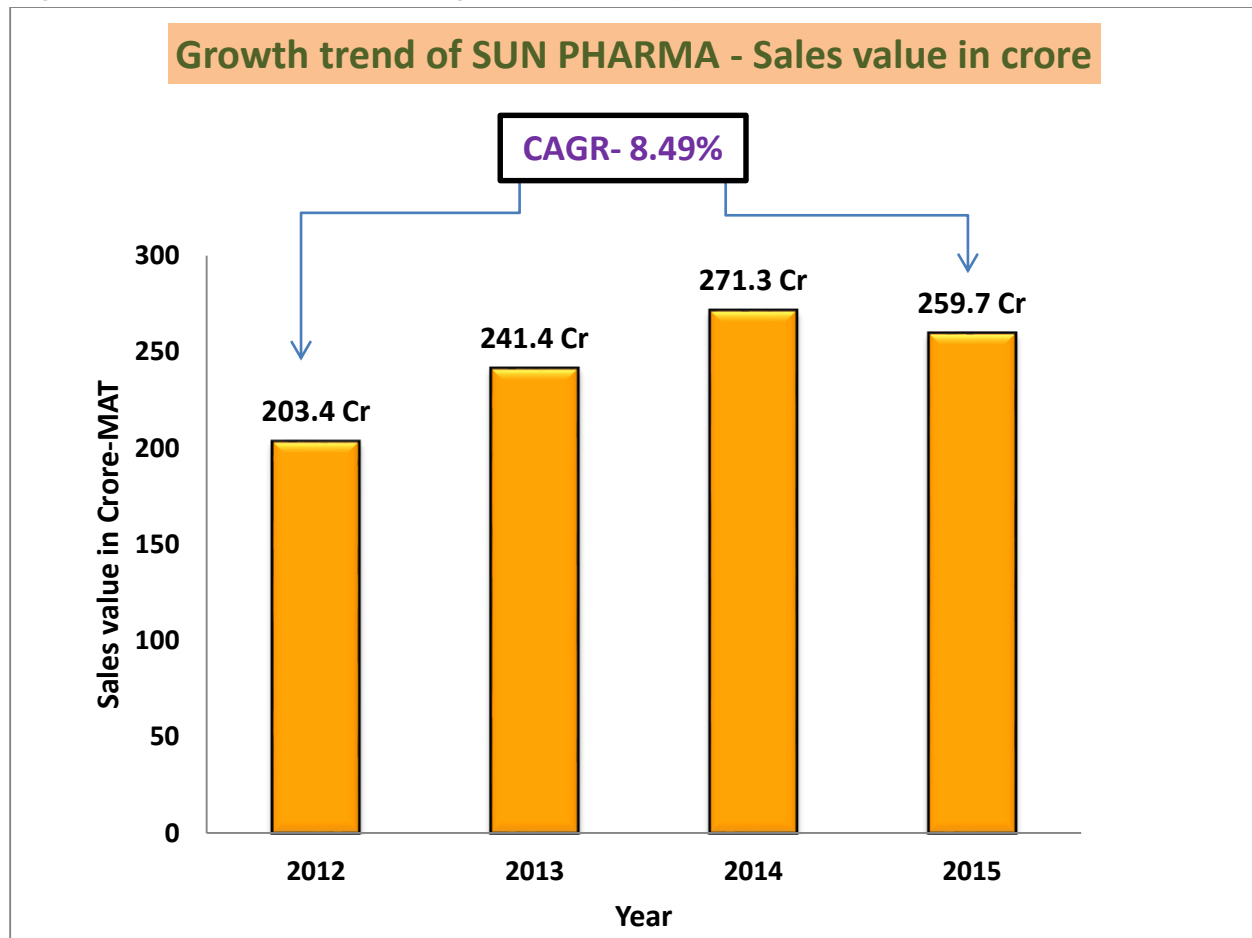


Interpretation:

Topical Analgesic segment is growing significantly with a CAGR of **12.45%** from Rs 536 Cr (2012) to Rs 762.5 Cr (2015) in terms of Sales value MAT. (Source: IMS data) .It can be calculated that the highest growth was measured between year 2012 to 2013 of 14%, which 2013-2014 year shows 12.8% increase and 2014-2015 shows 10.3% growth. Still on cumulatively the Topical Analgesic market is growing with respectable CAGR.

SUN PHARMA sales value trend in Topical Analgesic market from 2012 to 2015:

Figure: 3. (Source: IMS Base file 2011-2016)



Interpretation:

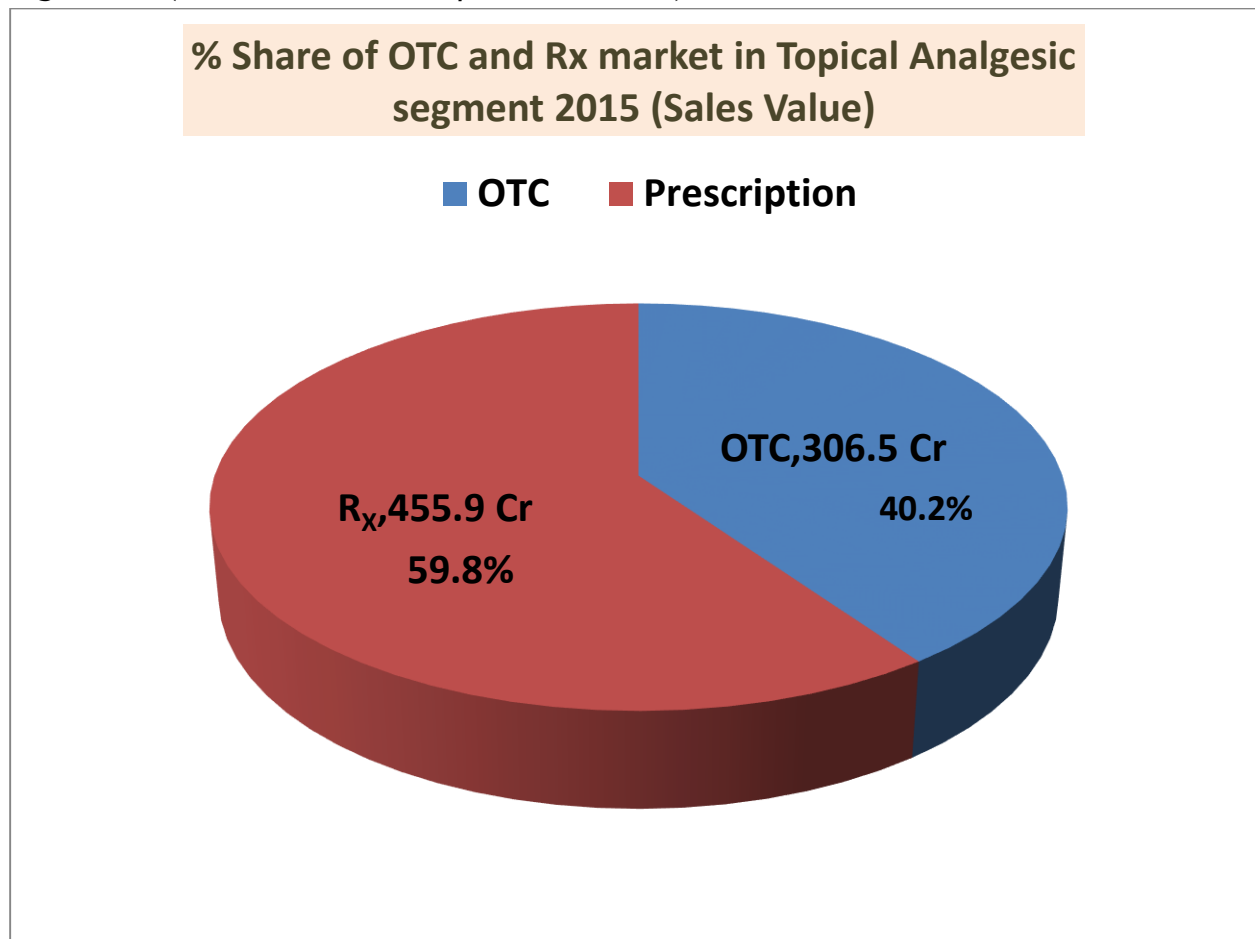
Sales value of SUN Pharmaceutical in 2015 was Rs 259 Cr which is 33.98% share of sales value among topical analgesic segment (Rs 762.4 Cr).

Also SUN Pharmaceutical is growing with a CAGR of 8.49% from 2012-2015 in Topical Analgesic segment, which is less than industry's CAGR but significantly worthy for future growth.

Between year 2012 to 2013, growth of SUN Pharmaceutical was 18.89%, which was much more than Industry's growth rate of 14%.

Share of OTC and Rx market in Topical Analgesic market 2015:

Figure: 4. (Source: IMS Base file 2011-2016)



Interpretation:

Among the Topical Analgesic market the share of Rx and OTC market in terms of Sales value 2015 are:

OTC segment	40.2 % (Rs 306.5 Cr)
Rx segment	59.8% (Rs 455.9 Cr)

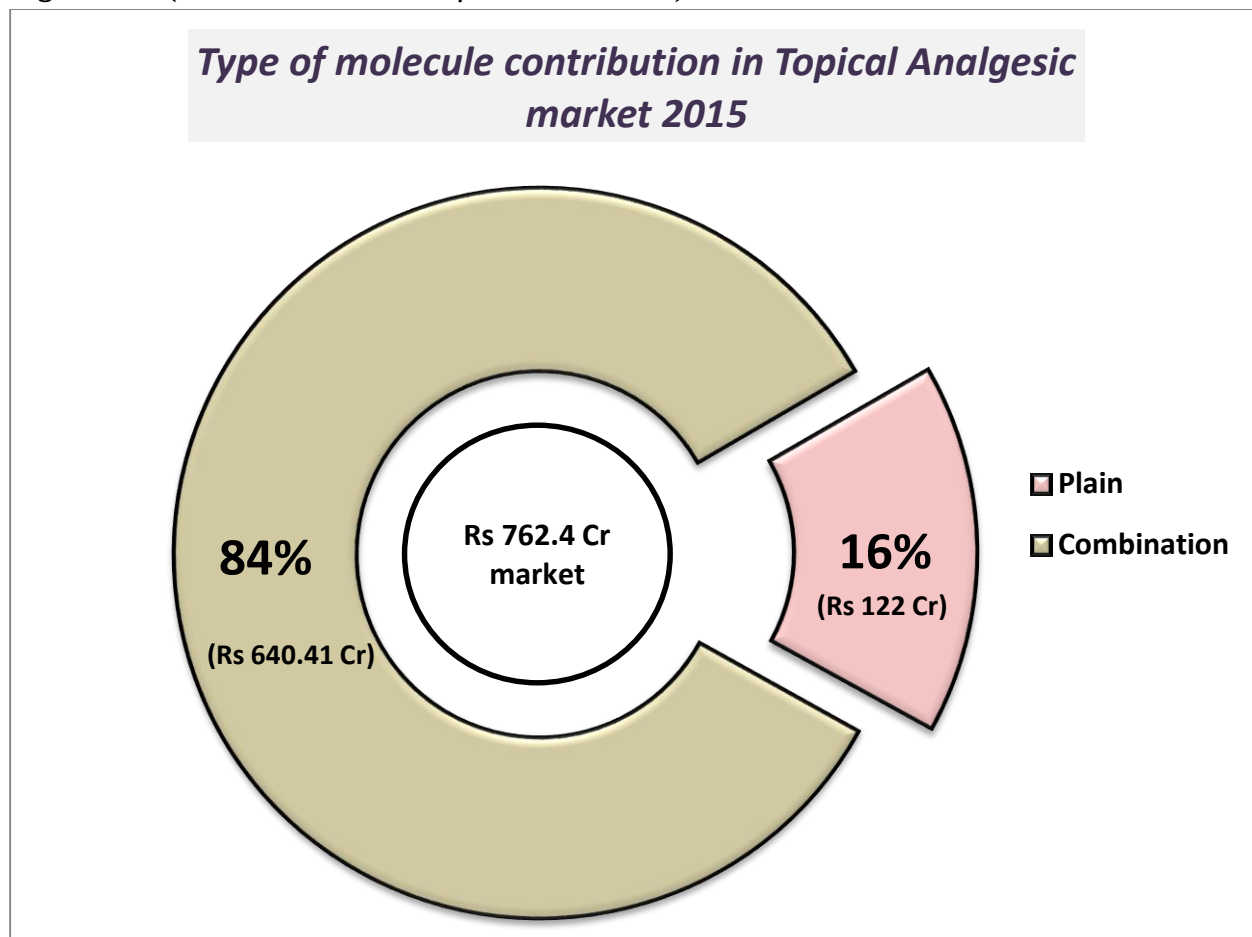
(Source: IMS data)

In OTC market of Topical Analgesic the top leaders (Brands) include Volini, Moov, Amrutanjan, Fast relief etc

But Volini has significantly highest share among OTC market of 78.5% (Rs 242.3 Cr) of Rs 306.5 Cr OTC Topical Analgesic market in 2015 (Sales Value).

Share of Type of molecule (Plain and Combination) in Topical Analgesic Segment 2015:

Figure: 5. (Source: IMS Base file 2011-2016)



Interpretation:

The % share of sales value of Combination molecule is 84% (Rs 640.41 Cr) and Plain molecule is 16% (Rs 122 Cr) in 2015 out of total of Rs 762.4 Cr.

This shows that most of the revenue earnings in Topical Analgesic segment Industry are through Combination molecule contribution.

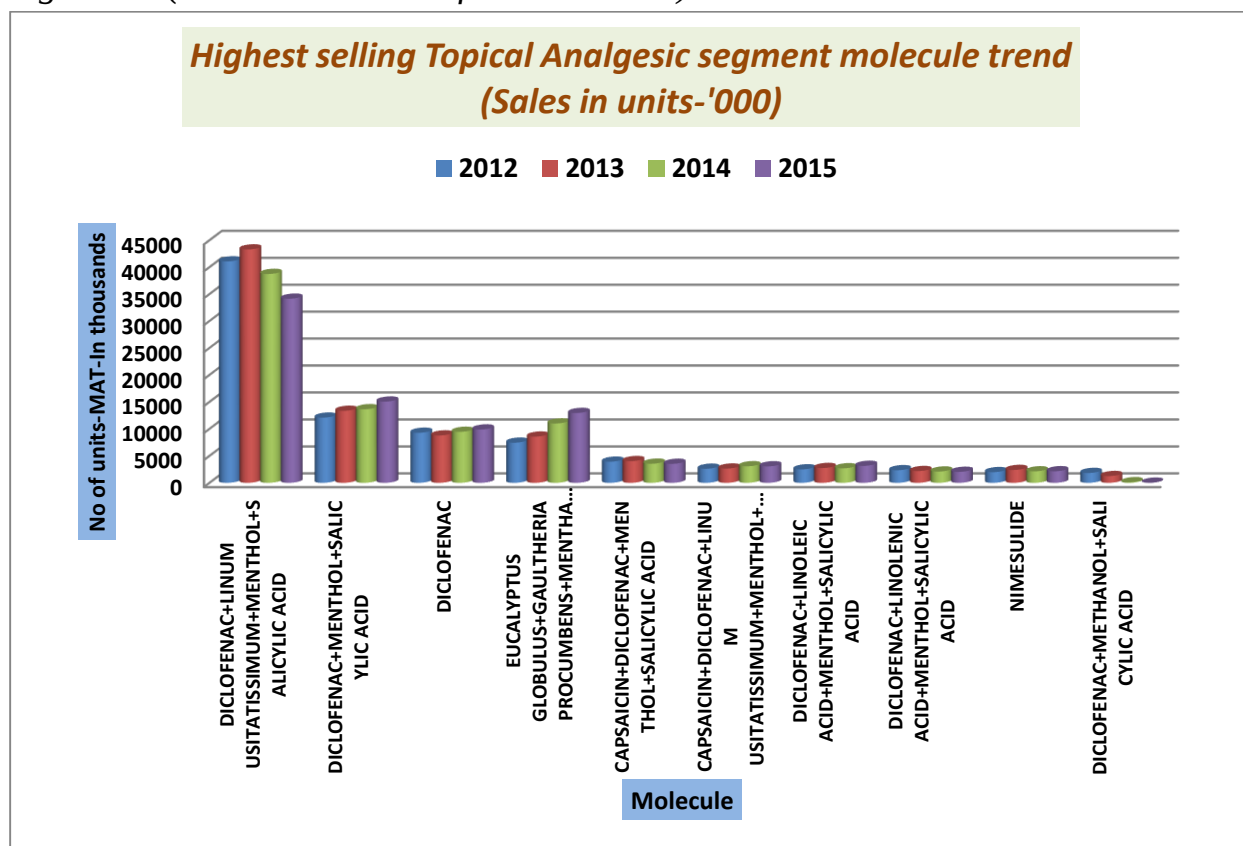
Example of molecules available in market:

Plain molecules: Diclofenac, Aceclofenac, Piroxicam, Flurbiprofen etc

Combination molecule: Diclofenac & combination, Nimesulide & combination, Etoricoxib & combination etc

Top selling molecules in years 2012-2015 and their growth trends:

Figure: 6. (Source: IMS Base file 2011-2016)



Interpretation:

It can be infer from the graph that the Top selling molecule is a combination molecule of Dilocfenac & combination. Only two out of all plain molecules are in top ten list of sales value: Diclofenac & Nimesulide

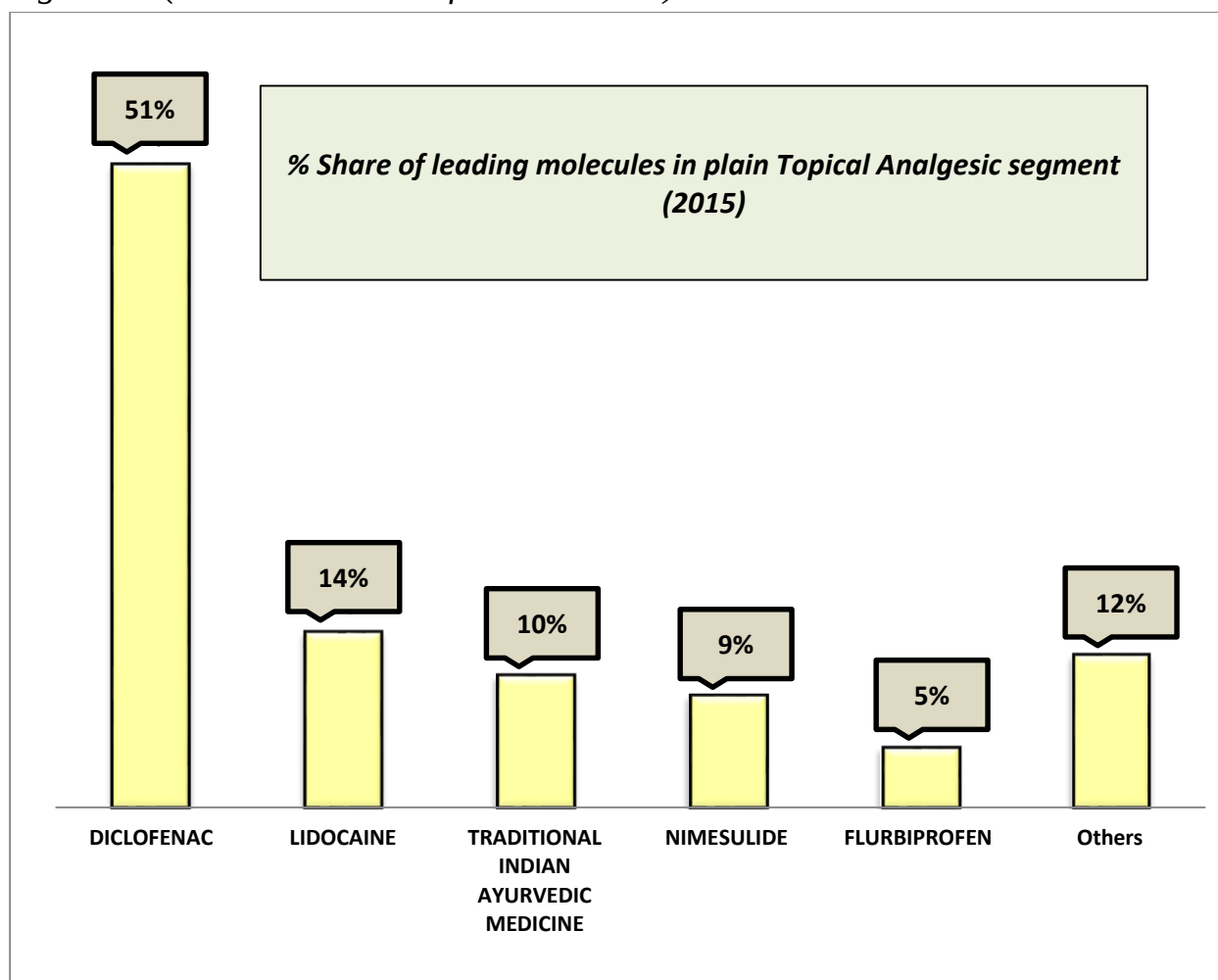
Others represent the dominance of Diclofenac & combination molecules in terms of sales value.

Molecule	Remarks
----------	---------

Diclo.+Linum Usitatissimum+Menthil+Salicylic acid	Decrease in sales from 2013 to 2015
Diclo.+Menthol+Salicylic acid	Continuous increase in sales from 2013 to 2015
Eucalyptus Globulus+Gaultheria procumbens+Mentha piperita etc	Fastest growing molecule from 2013 to 2015 among top ten molecules.

Top molecule contribution of share in Plain molecule sales value 2015:

Figure: 7. (Source: IMS Base file 2011-2016)



Interpretation:

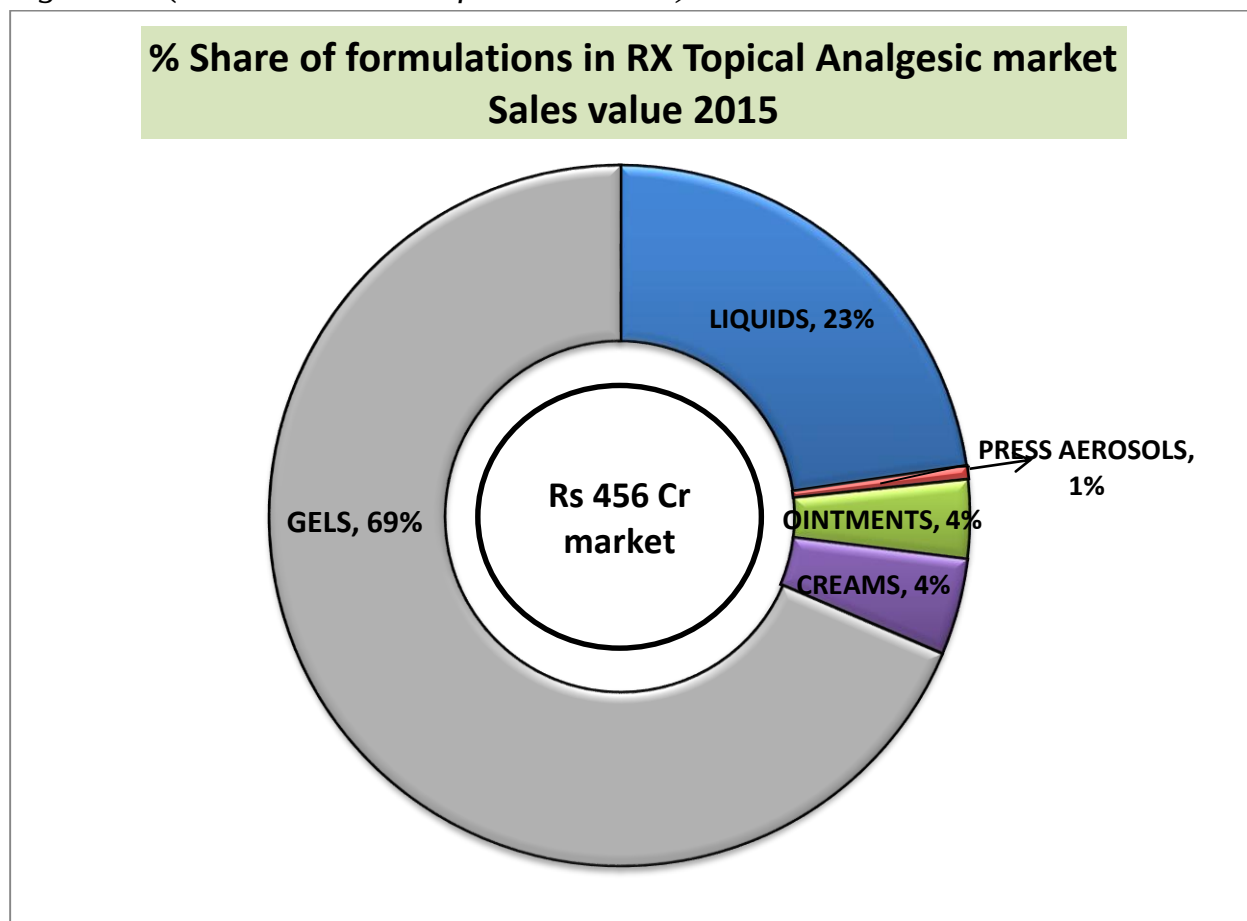
Diclofenac in plain molecules also is dominant in % share of plain molecule in terms of sales value 2015.

Top leading molecules of plain segment in sales value includes Lidocaine, Traditional Indian Ayurvedic med., Nimesulide, Flurbiprofen etc

We can see that, NSAID's contributes to 3 molecules among top five plain molecules. Local Anesthetic (Lidocaine) is second highest share holder (14%) in plain molecule segment in terms of sales value 2015.

Share of different formulations in Prescription Topical Analgesic segment in terms of Sales Value 2015:

Figure: 8. (Source: IMS Base file 2011-2016)



Interpretation:

Gels contribute to significantly highest (69 %) of sales value among Prescription Topical Analgesic formulation in 2015 indicating the market for Gel has higher potential for growth and to maximize the sales value.

Liquid on contrary has 23% sales value share among topical analgesic segment with second highest share value.

Leading brands, their market share and CAGR (growth) in Topical Analgesic segment:

Table: 1. (Source: IMS Base file 2011-2016)

Rx Topical Analgesic Top leading brands (2015)			
Brands	Sales Value 2015 (Lacs)	Market Share%	CAGR % (2012-2015)
VOVERAN (Novartis)	4018.34	8.8%	9%
D.F.O (Ozone Pharma)	2155.01	4.7%	24%
OXALGIN (Zydus Cadila)	2150.87	4.7%	15%
VOLITRA (SUN Pharma)	1749.07	3.8%	3%
DYNAPAR QPS (Troikaa)	1608.08	3.5%	113%
LOX (Neon Labs)	1466.56	3.2%	11%
RUMALAYA (Himalaya)	1286.11	2.8%	16%
NOBEL (Mankind)	1255.22	2.8%	13%
LAL TAIL (Dabur India)	1184.34	2.6%	24%
OMNI (Cipla)	1150.54	2.5%	5%

Market share & CAGR (growth) in different Strengths of Rx Diclofenac & combination Gel 2015: Table: 2.

Rx Topical Gel/sols leading % strengths (Diclofenac & Comb.) 2015			
Strength of Gel/sols	Sales Value 2015 (Lacs)	Market Share% (2015)	CAGR (%) 2012-2015
1.16%	2680.3	13.18%	9%
1%	2027.8	9.97%	21%
0.24%	253.4	1.25%	10%
2%	201.5	0.99%	64%
4%	51.9	0.26%	148%
3%	2.4	0.01%	-28%
(Blank)	15118.5	74.34%	16%

Competitor Analysis:

The Leading Brands in Prescription Topical Anti-Inflammatory & Analgesic Diclofenac Gel segment with their Market share, SKU's, CAGR%, product launch date, Price and sales value 2012-2015.

Table: 3. (Source: IMS Base file 2011-2016)

Rx Topical gel in Diclofenac & com. Molecule								
Brands	Sales Value in Crore (Rs)				%Market share 2015	CAGR (%) 2012-2015	Product launch	Years till now
	2012	2013	2014	2015				
VOVERAN(Novartis)	31.4	31.2	34.8	40.2	20%	9%	Feb-86	30
D.F.O (Ozone pharma)	11.2	14.6	17.6	21.6	11%	24%	Jan-01	15
OXALGIN (Zydus Cadila)	14.3	16.4	18.6	21.5	11%	15%	Dec-09	7
VOLITRA (SUN PHARMA)	14.5	14.4	16.8	16.2	8%	4%	Jan-07	9
NOBEL (Mankind)	8.7	9.9	10.2	12.6	6%	13%	Aug-03	13
OMNI (Cipla)	9.9	10.1	10.3	11.5	6%	5%	Nov-99	17
POWERGESIC (Jenburkt)	6.0	6.4	7.3	7.7	4%	9%	Dec-98	18
RELAXYL (Franco Indian)	3.6	4.6	6.1	6.4	3%	21%	Aug-93	23
DYNAPAR (Troikaa)	3.5	3.7	3.9	4.5	2%	9%	Jan-99	17
NANOFAST (Pharmed)	1.1	2.0	3.2	3.9	2%	51%	Aug-11	5

Interpretation:

The market leader in prescription Topical Diclofenac & combination Gel is Voveran of Novartis Company with significantly highest market share of ~ 20% (In terms of Sales value 2015). Following Voveran are the two brands D.F.O and Oxalgin with ~11% share. But Oxalgin would be considered better in terms of late product launch than D.F.O but having same share of ~11%. Volitra of SUN pharmaceuticals has share of 8% in terms of sales value 2015 and is followed by others brands like Nobel, Omni, Powergesic, Relaxyl, Dynapar and Nanofast among top ten. The highest CAGR among top ten brands in Diclofenac & combination gel prescription market from 2012-2015 is of NanoFast (51%). Also CAGR above 20% is attributed to two more brands named: D.F.O (24%) and

Relaxyl (21%). Since the CAGR of NanoFast is 51%, hence this could be one of the reason for it to achieve the 2% market share in 2015 in just five years in Topical Diclofenac and combination gel prescription market.

Details of Price, no of units sold, SKU's and CAGR% of Top five competitive brands in prescription Topical Anti-Inflammatory & Analgesic market.

Table: 4.(Price taken from Online site : Medplus mart).

Competitor Brands in Prescription Topical Analgesic Gel (Diclofenac & comb)							
Brands	SKU	Price (MRP - Rs)	No of units sold (In thousand)				CAGR% (Units sold)
			2012	2013	2014	2015	
VOVERAN	VOVERAN EMULGEL 1.16 % 30 G x 1	86.75	2,368	2,175	1,965	1,992	-6%
	VOVERAN EMULGEL 1 % 21 G x 1	69.20	1,379	1,467	1,418	1,432	1%
	VOVERAN THERMAGEL 30 G x 1	109.00	820	759	732	762	-2%
	VOVERAN EMULGEL 1.16 % 50 G x 1	173.99	789	721	744	696	-4%
	VOVERAN-TPM GEL 1.16 % 30 G x 1	105.45	0	0	368	642	75%
D.F.O	D.F.O GEL 30 G x 1	79.00	2,671	2,726	2,651	2,952	3%
	D.F.O NANO GEL 1 % 30 G x 1	79.00	3	149	239	256	336%
	D.F.O GEL 50 G x 1	100.00	0	1	128	249	1773%
OXALGIN	OXALGIN NANO GEL 30 G x 1	90.00	2,560	2,626	2,694	3,018	6%
	OXALGIN NANO GEL 50 G x 1	147.00	0	0	21	59	178%
OMNI	OMNI GEL 30 G x 1	79.00	3,858	3,973	4,054	4,152	2%
	OMNI GEL 10 G x 1	36.50	2,749	2,951	2,643	2,924	2%
	OMNI HOT GEL 30 G x 1	79.50	108	163	204	194	22%
NOBEL	NOBEL GEL 10 G x 1	22.38	2,021	2,258	2,230	2,681	10%
	NOBEL GEL 30 G x 1	55.66	2,127	2,167	1,999	2,202	1%
	NOBEL GEL 20 G x 1	-	2	0	0	0	-100%

Interpretation:

The highest no of units sold in prescription Topical Analgesic gel segment in 2015 was of Omni Gel 30G (4152000 units sold), with a price of Rs 79/unit. Voveran which is market leader in Rx topical Analgesic Gel segment has maximum no of units sold of SKU (Voveran Emulgel 1.16% 30g) followed by 21 G Gel. Both the SKU's of OMNI gel brand are sold above 2200000 units /year (2015), is not the leader in market share of value, due to its lower price (30G = Rs 55.66 & 10G = Rs

22.38). The highest sold SKU among all the brand was of 30G except Nobel Gel whose highest sold SKU was of 10G with least price (Rs 22.38) among top five brands.

Prescriber Analysis:

Table 5.(SMSRC Rx data)

% share of specialities in <u>Diclofenac comb.gel</u> , <u>Top. NSAIDs spray</u> & <u>Top. NSAIDs Ayuv. gel</u> and their preferred brands				
<u>ORTHOPAEDIC (33%)</u> Top three brands : <i>OXALGIN nanogel, VOLITRA gel, SYSTAFLAM gel</i>		<u>GENERAL PRACTITIONER (24%)</u> Top three brands : <i>VOLINI gel, OXALGIN nanogel, VOVERAN emulgel</i>		
<u>CONSULTING PHYSICIAN (10%)</u> Top three brands : <i>VOLINI gel, DFO gel, VOVERAN emulgel</i>	<u>GEN. SURGEON (7%)</u> Top three brands: <i>VOLINI gel, VOLITRA gel, VOVERAN emulgel</i>	<u>RURAL DOCS. (7%)</u> Top three brands: <i>NOBEL gel/oint, VOLINI gel, OMNI gel</i>	<u>GYNAEC (6%)</u> Top three brands: <i>VOLINI gel, VOVERAN emulgel, SYSTAFLAM gel</i>	<u>OTHERS (14%)</u>

About 1/3 of the total prescriptions of topical Diclofenac & Comb. Gel are prescribed by Orthopaedic doctors with most preferred brands as Oxalgin, Volitra and Systafam. G.P contributes to 24% and C.P contributes to 10% of the total topical Diclofenac & Comb. Gel prescriptions, both together contributes to 34% of the total prescription (1/3 of total Rx). Also both G.P's and C.P's prescribe Volini

Gel, denoting that inspite of OTC category Volini is still prescribed Topical Analgesic gel by G.P', C.P's, Gen.Surgeon, Rural doc's, Gynaec etc.

4. Primary Research (Field Research)

RESEARCH TITLE:

A STUDY ON NEED AND AWARENESS OF TOPICAL ANTI-INFLAMMATORY
& ANALGESIC GELS CONTAINING HIGHER CONCENTRATION
DICLOFENAC AMONG DOCTORS

Research objectives:

1. PRIMARY OBJECTIVES:

- a. To find out the Need and Awareness about higher concentration Topical Anti-Inflammatory & Analgesic Gels among doctors.

2. SECONDARY OBJECTIVES:

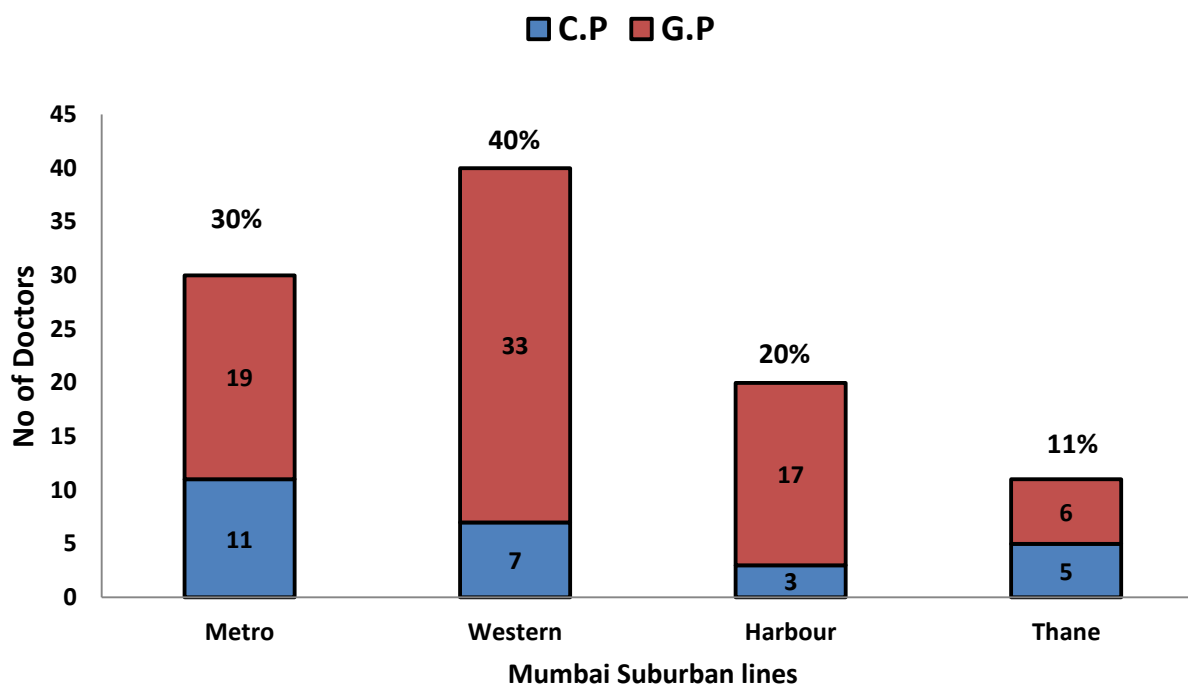
- a. To understand the prescription behavior of doctors in Topical Anti-Inflammatory & Analgesic gels.
- b. To understand the Perception's of doctors about Topical Anti-Inflammatory & Analgesic gels.

Research methodology:

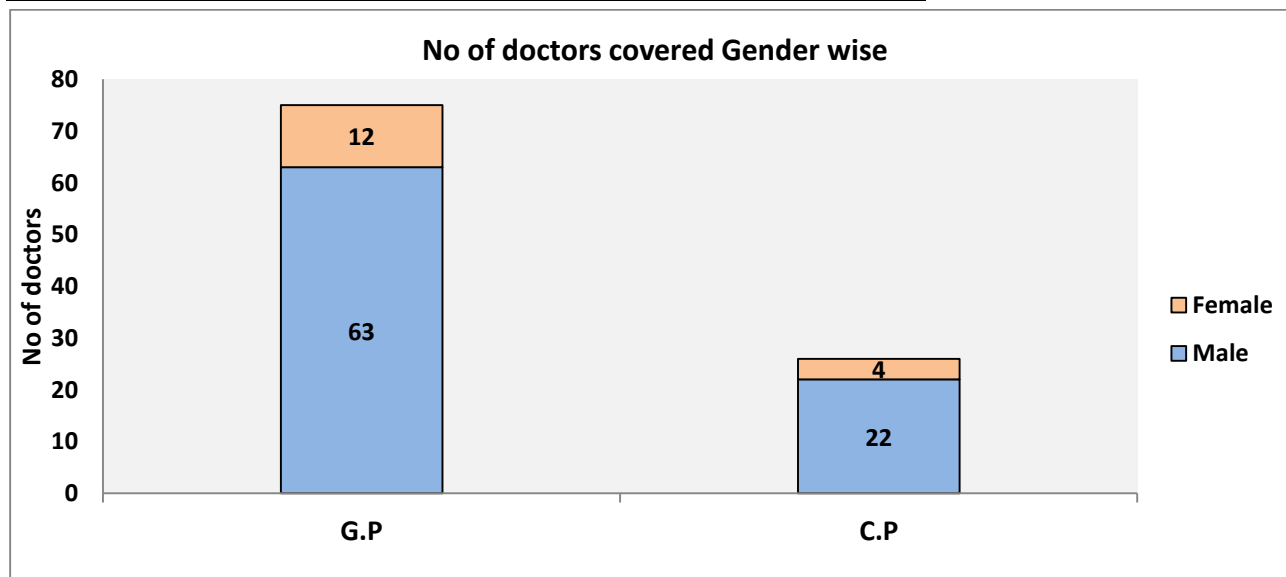
<u>PARAMETERS</u>	<u>DESCRIPTIONS</u>
Research Type	Exploratory Research
Type of Data	Primary data
Data collection tool	Structured Questionnaire (Open ended & Close ended) & Discussion
Study area	Mumbai, India
Sample size	101 Doctors
Sampling	Convenience sampling
Respondents	General Physician (G.P - 75) and Consulting Physician (C.P - 26)
Analysis tool	MS Excel 2007
Analysis representation	Charts, Graphs and Tables

AREA'S COVERED FOR PRIMARY DATA COLLECTION:

Speciality of Doctors covered under Mumbai Suburban Lines



PROPORTION OF DOCTORS COVERED GENDER WISE:

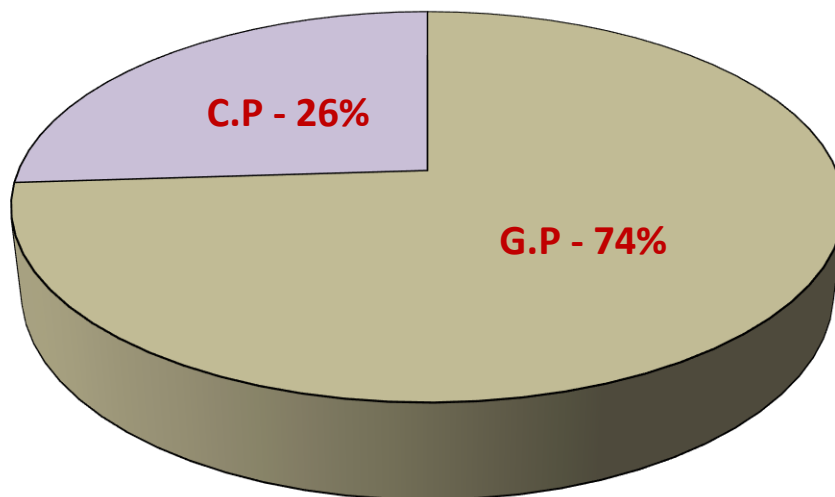


% OF DOCTORS COVERED SPECIALITY WISE:

% share of speciality covered in study sample

■ G.P - (75/101)

■ C.P - (26/101)



4.1. Analysis & interpretation:

ANALYSIS AND INTERPRETATION OF PRIMARY DATA COLLECTED FROM GENERAL PHYSICIAN (75) & CONSULTING PHYSICIAN (26) DOCTORS

Q.1) Doctor, what are the numbers of pat. Of Musculoskeletal Disorders (e.g. Low back pain/Joint Pain/Arthritis and related disorders) do you treat per day?

Chart.PR.1

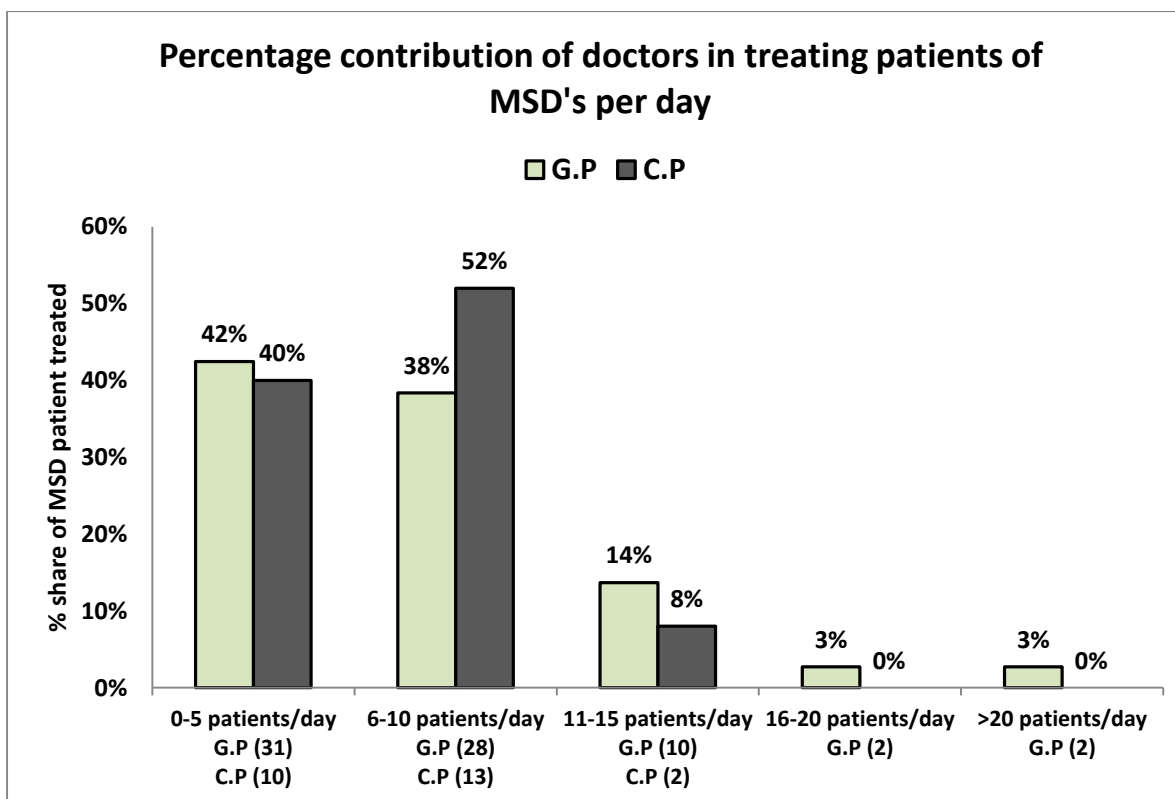


Table.PR.1

Speciality (Responded sample size)	Number of MSD patients treated/Day	Average no of patients treated/Doctor/Day	Min. no of patients treated by a Doctor/Day	Max. no of patients treated by doctor/day	STDev in no of patients treated by speciality per day
G.P (73)	506	6.93	0-1	20	4.46
C.P (25)	163 – 164	6.54	1-2	15	3.65

Total no of respondents of Q.1) = **98** (G.P – **73** and C.P – **25**)

INTERPRETATION:

Graph.PR.1:

- ❖ According to findings (Graph.PR.1), majority of C.P's treat 6-10 MSD patients per day.
- ❖ 42% of G.P's treat 0-5 MSD patients per day, 38% of G.P's treat 6-10 patients per day.
- ❖ Also 14% of G.P's treat 11-15 MSD patients per day, where 8% of C.P treats 11-15 patients per day.

Table.PR.1:

- ❖ Average number of MSD patients treated by a G.P per day is 6.93, almost equivalent to 7 patients per day
- ❖ Average number of MSD patients treated by C.P per day is 6.54, almost equivalent to 13 patients per two days.
- ❖ The distribution of number of MSD patients treated by C.P and G.P per day is nearly same.(C.P-6.54 Avg pat./day and G.P- 6.93 Avg pat./day)

Q.2) Doctor, Out of the above number of patients treated how many patients do you prescribe Topical Anti-Inflammatory & Analgesic Gel?

Chart.PR.2

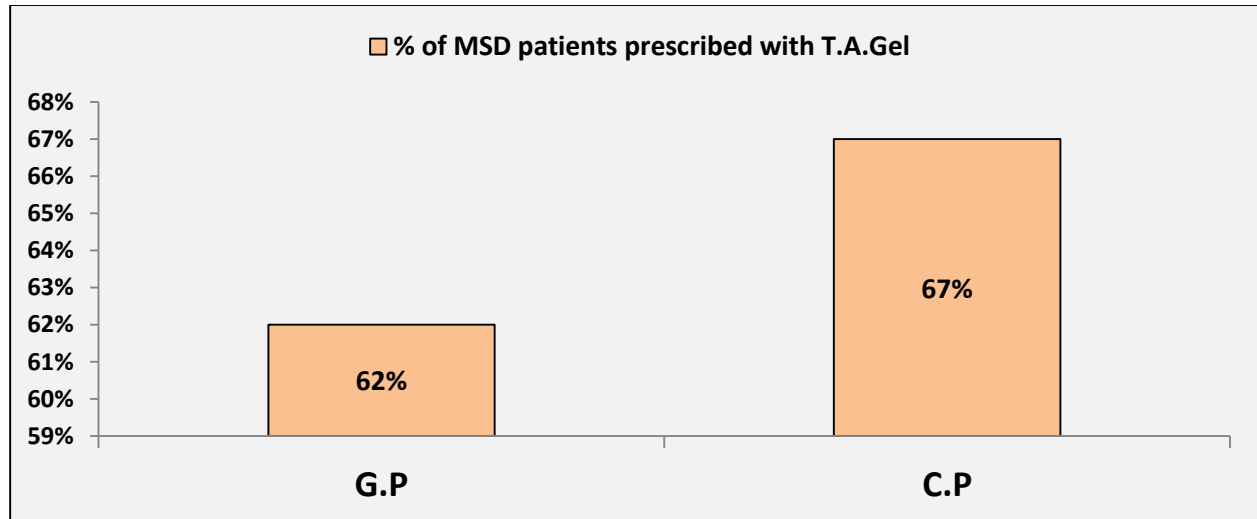


Table.PR.2

Speciality (Responded sample size)	Number of MSD patients treated/Day	Number of MSD patients Prescribed with T.A gel /Day	Average % of MSD patients prescribed with T.A. gel
G.P (73)	506	314 - 315	62%
C.P (25)	163 - 164	110	67%

Total no of respondents = 98 (G.P – 73, C.P – 25)

INTERPRETATION:

- ❖ Of all the MSD patients treated, C.P prescribes maximum percentage (**67%**) of MSD patients with Topical Anti-Inflammatory and Analgesic Gel.
- ❖ G.P prescribes **62%** of treated MSD patients with Topical Anti-Inflammatory and Analgesic Gel.

Q.3a) Doctor, which molecules you prefer in Topical Anti-Inflammatory & Analgesic Gel?

Table.PR.3

(Rank) Molecule	G.P	C.P	Total Doctors	Molecule prescribed by % of doctors
(Rank 1) Diclofenac & Comb.	71	26	97	100%
(Rank 2) Capsicum& Comb.	6	4	10	10%
(Rank 3) Piroxicam & Comb.	5	2	7	7%
(Rank 4) Mephenesin & Comb.	5	1	6	6%
(Rank 5) Ayurvedic	3	2	5	5%
(Rank 5) Methyl Salicylate & Comb.	4	1	5	5%
(Rank 7) Ibuprofen	3	1	4	4%
(Rank 8) Nimesulide & Comb.	2	1	3	3%
(Rank 8) Indomethacin	1	2	3	3%
(Rank 10) Felbinac	1	1	2	2%
(Rank 10) Oleum lini & Comb.	1	1	2	2%
(Rank 12) Flurbuprofen	1	0	1	1%
(Rank 12) Aceclofenac	1	0	1	1%

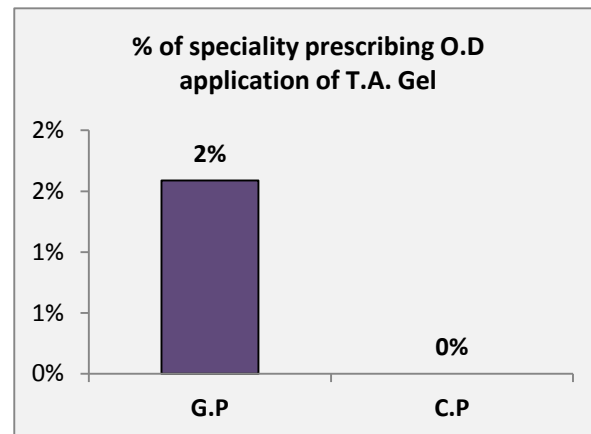
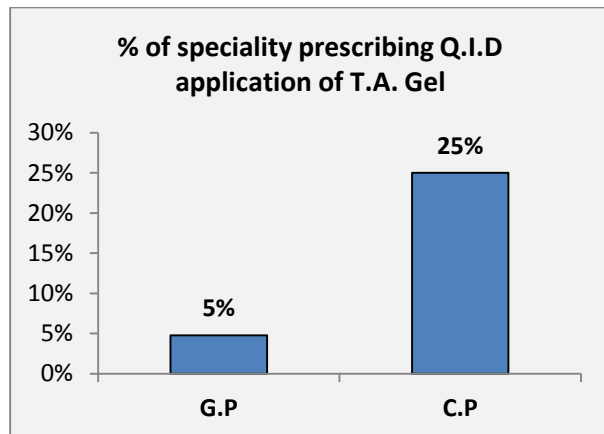
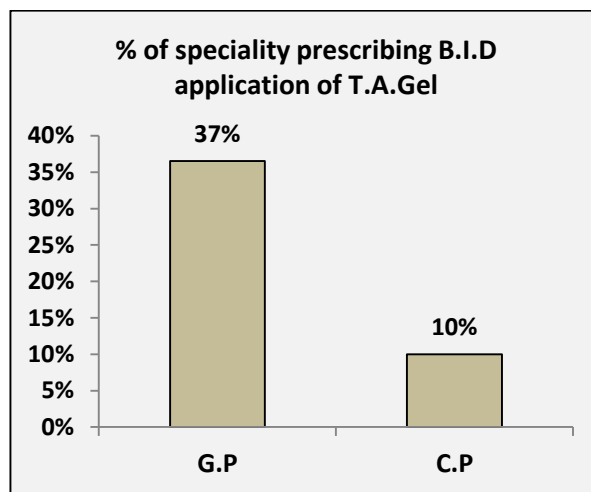
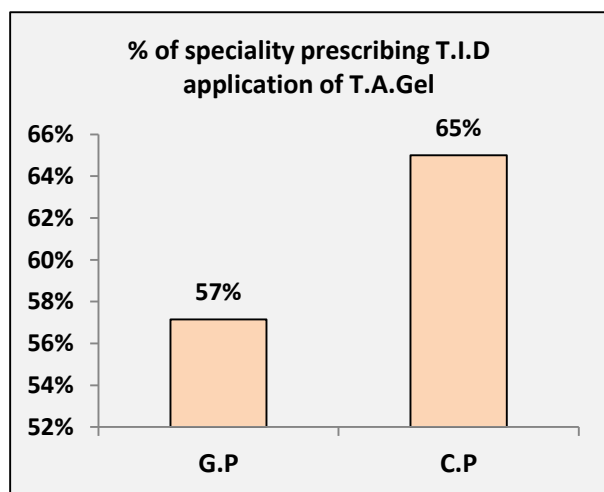
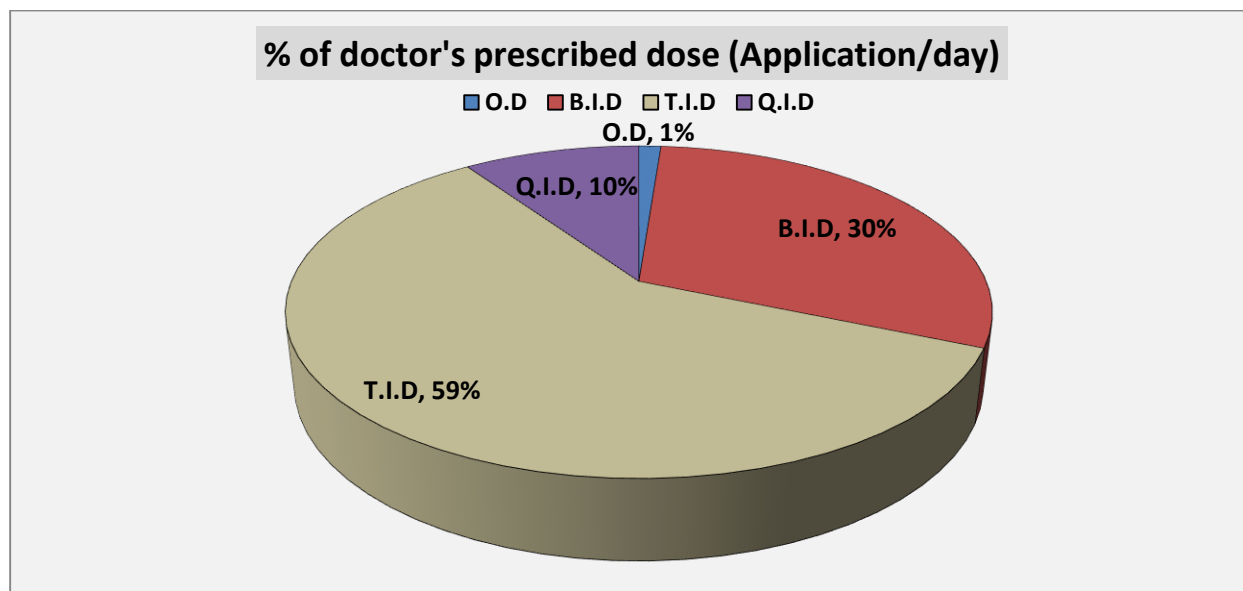
Total respondents: 97 (G.P-71, C.P-26)

INTERPRETATION:

- ❖ **100%** of the responded doctors (97 doctors) prefer **Diclofenac & Combination** as their first preference in Topical Anti-Inflammatory & Analgesic Gel.
- ❖ Out of 97 doctors, **10%** of the doctors prefer **Capsicum & Combination molecule** in Topical Anti- Inflammatory & Analgesic Gel.

- ❖ Similarly 7% of doctors prefer Piroxicam & combination molecule in Topical Anti- Inflammatory & Analgesic Gel and others molecule includes Mephenesin & comb. (6%), Ayurvedic (5%), Methyl Salicylate & comb. (5%) and so on with total 13 molecules responded by 97 doctors.
- ❖ The result shows that most significantly preferred molecule in Topical Anti-Inflammatory & Analgesic Gel is **Diclofenac & Combination (100%)**.

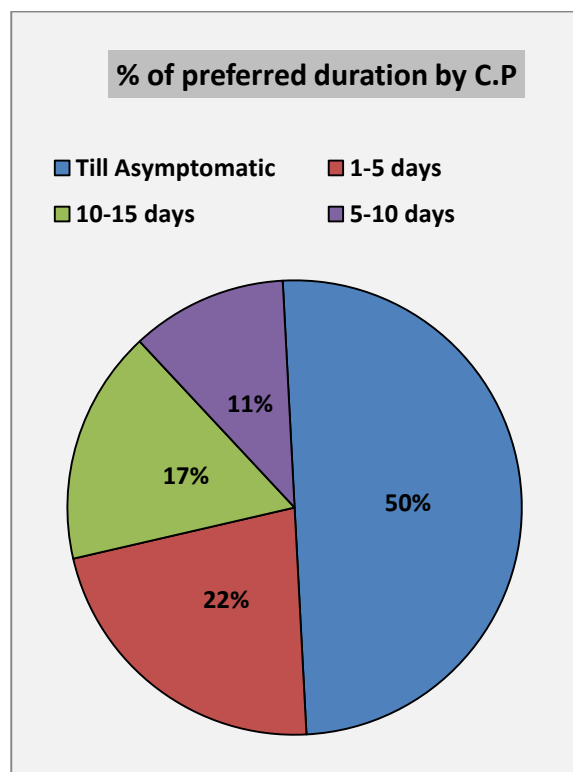
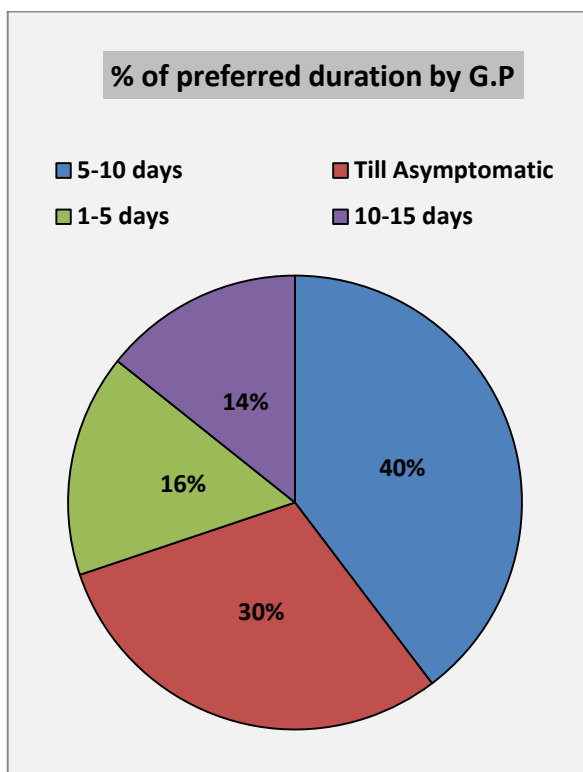
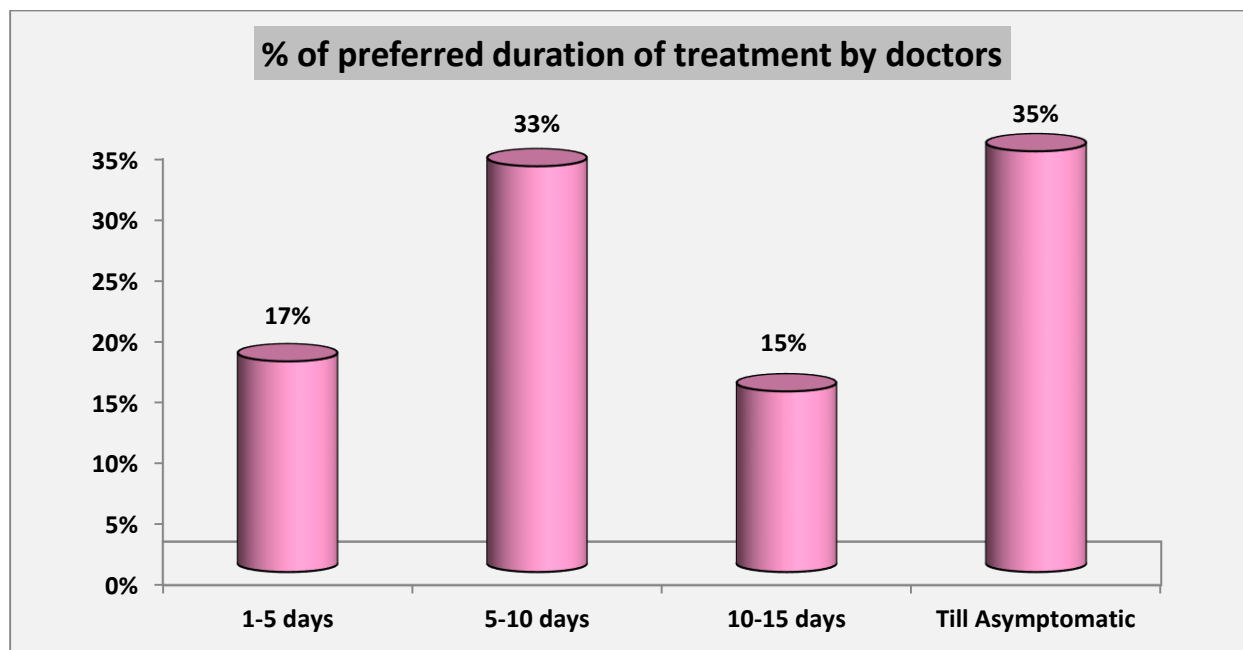
Q.3b) Doctor, what is the number of application of T.A. Gel you prefer to prescribe the most?



INTERPRETATION:

- ❖ Majority of doctors (59%) prefer dose of T.I.D application of T.A. Gel.
- ❖ Second preferred dose of application of T.A. Gel by doctors is B.I.D with 30% of doctors preferring B.I.D.
- ❖ Only 10% and 1% of doctors prefer Q.I.D and O.D application of T.A. Gel respectively.
- ❖ 65% of C.P and 57% of G.P prefer T.I.D application of T.A. Gel contributing maximum percentage of individual speciality.
- ❖ G.Ps (37%) prefers B.I.D application of T.A. Gel more than C.P (10%).
- ❖ Q.I.D application of topical Analgesic Gel is preferred more by C.Ps (25%) than G.Ps (5%).
- ❖ Overall both the specialties (G.Ps & C.Ps) prefer T.I.D application of Topical Anti-Inflammatory & Analgesic Gel the most.

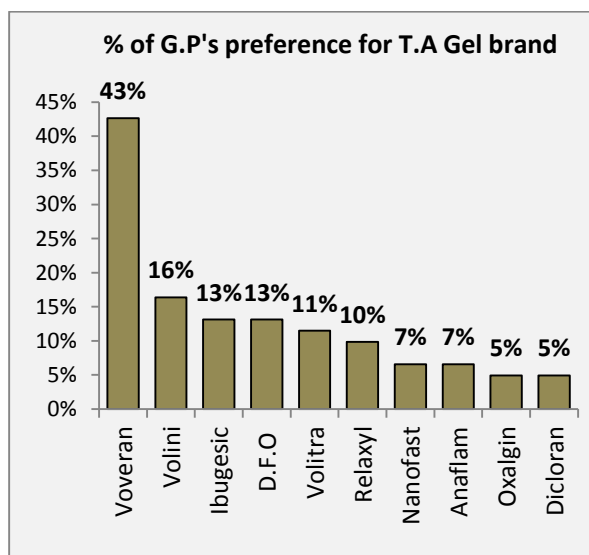
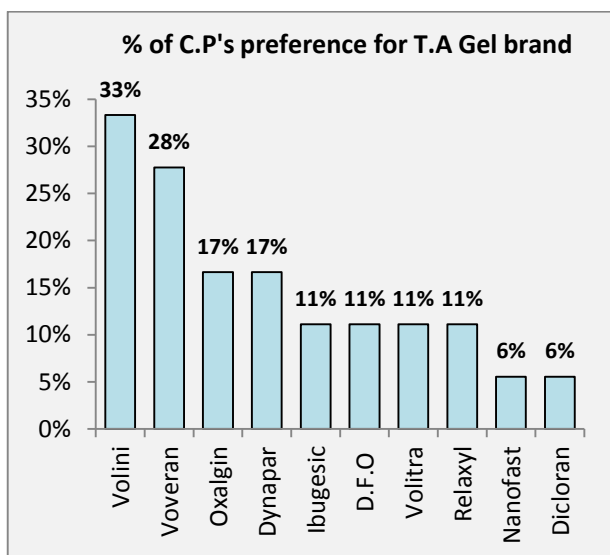
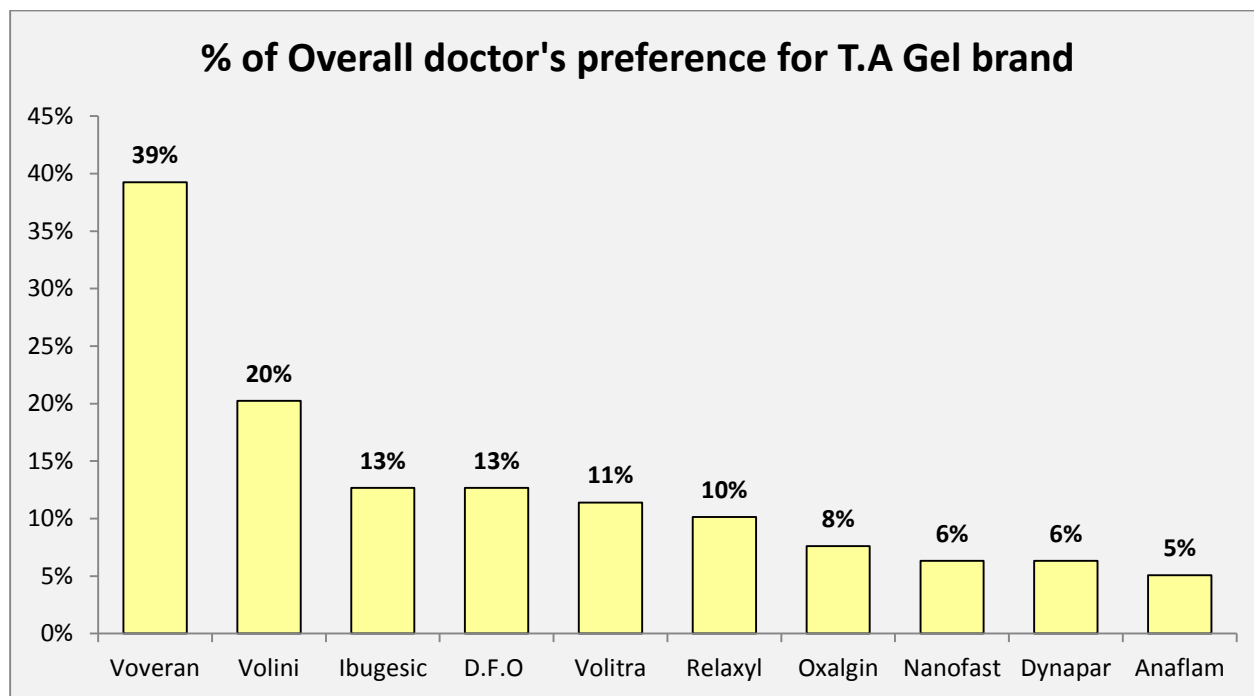
Q.3c) Doctor, what is the duration of therapy you prefer to prescribe for Topical Anti-Inflammatory & Analgesic Gels?



INTERPRETATION:

- ❖ Of all the doctors, 35% of doctors prefer the duration of treatment with T.A Gel as “Till Asymptomatic” (i.e. Patient should apply T.A Gel till pain goes away).
- ❖ Also (30%) almost 1/3rd of the doctors prefer the duration of treatment of T.A. gel for 5-10 days.
- ❖ Only 17% and 15% of the doctor prefer the duration of treatment with T.A Gel to be 1-5 days and 11-15 days respectively.
- ❖ Most preferred duration of treatment with T.A Gel by G.Ps (40%) is 5-10 days followed by 30% G.Ps preferring duration as “Till Asymptomatic”.
- ❖ Most preferred duration of treatment with T.A Gel by C.Ps is “Till Asymptomatic” with 50% (1/2 of C.Ps) C.Ps, which is followed by 1-5 days duration of treatment preferring about 22% C.Ps.

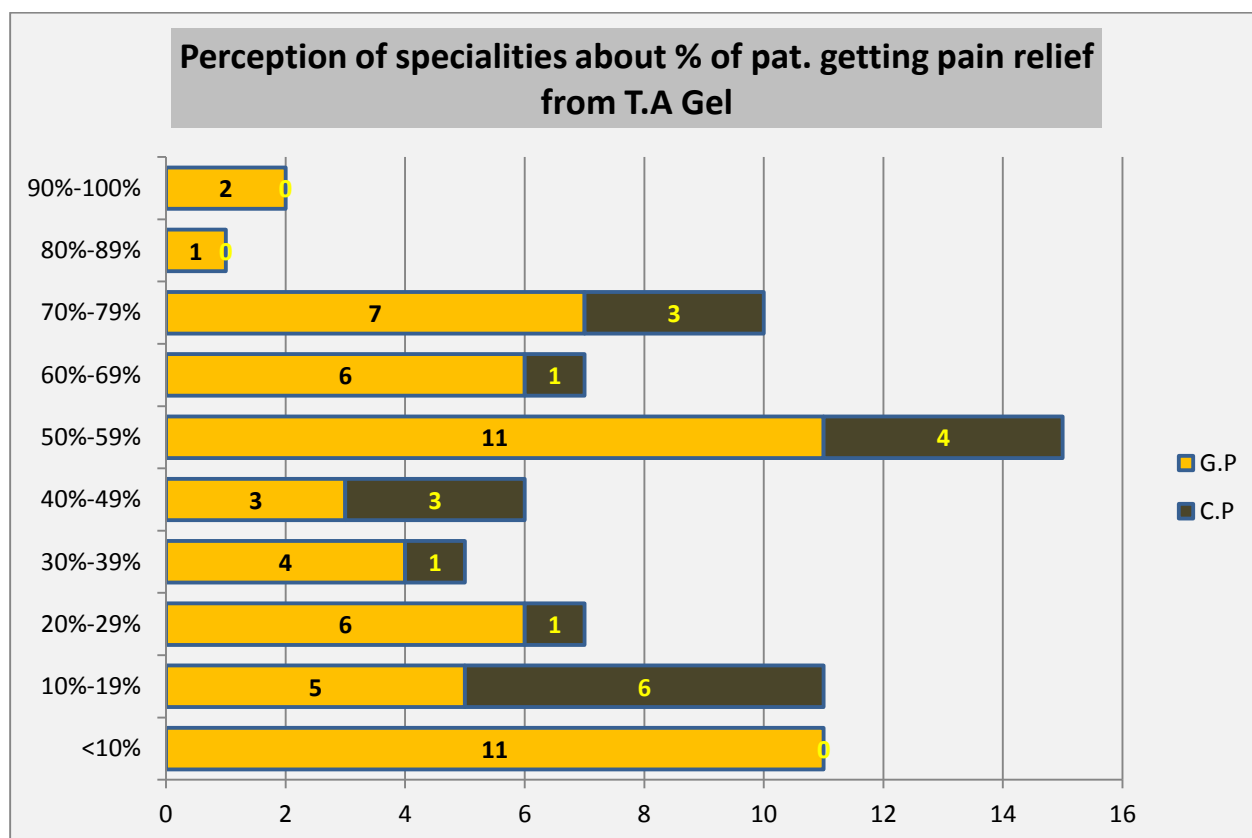
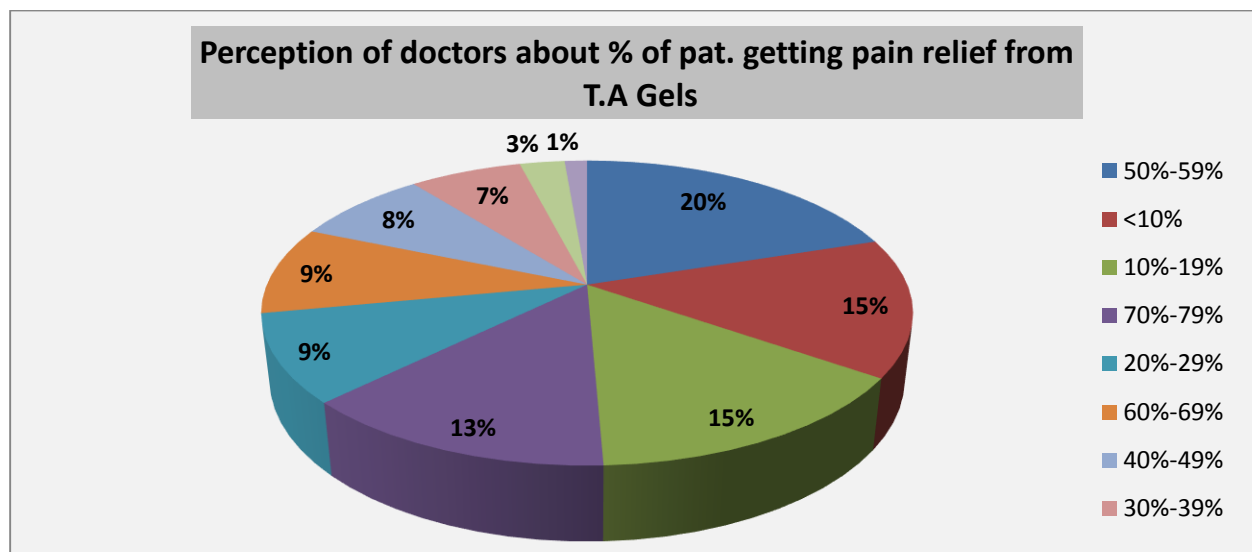
Q.4) Doctor, which are the brands you prescribe most in Topical Anti-Inflammatory & Analgesic Gels?



INTERPRETATION:

- ❖ Out of overall responded doctors, majority of them preferred Voveran as the most preferred brand with 39% of doctors prescribing Voveran; it is followed by second most preferred brand as “Volini” (20%) in Topical Anti-Inflammatory & Analgesic Gel.
- ❖ Most preferred brand by C.P’s is “Volini” with 33% of C.P’s prescribing it. Voveran (28%) is second preferred brand by C.Ps.
- ❖ This signifies C.P’s are potential customers for Volini in prescribing Topical Anti-Inflammatory & Analgesic Gel.
- ❖ G.P’s most preferred brand is Voveran (43%) followed by Volini (16%). G.P’s should be focus more in terms of targeting and positioning new product.

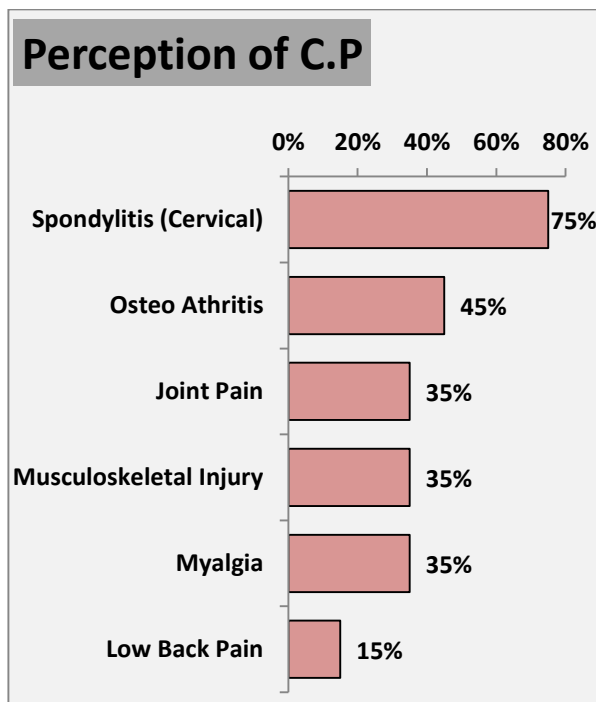
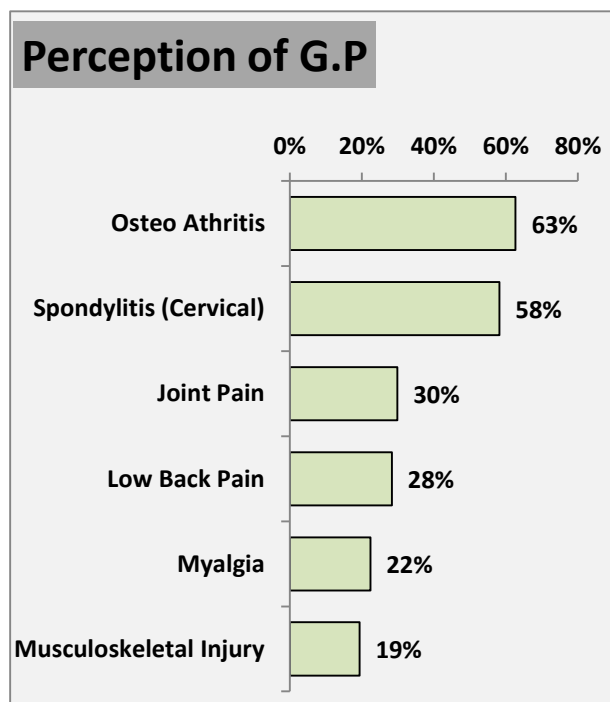
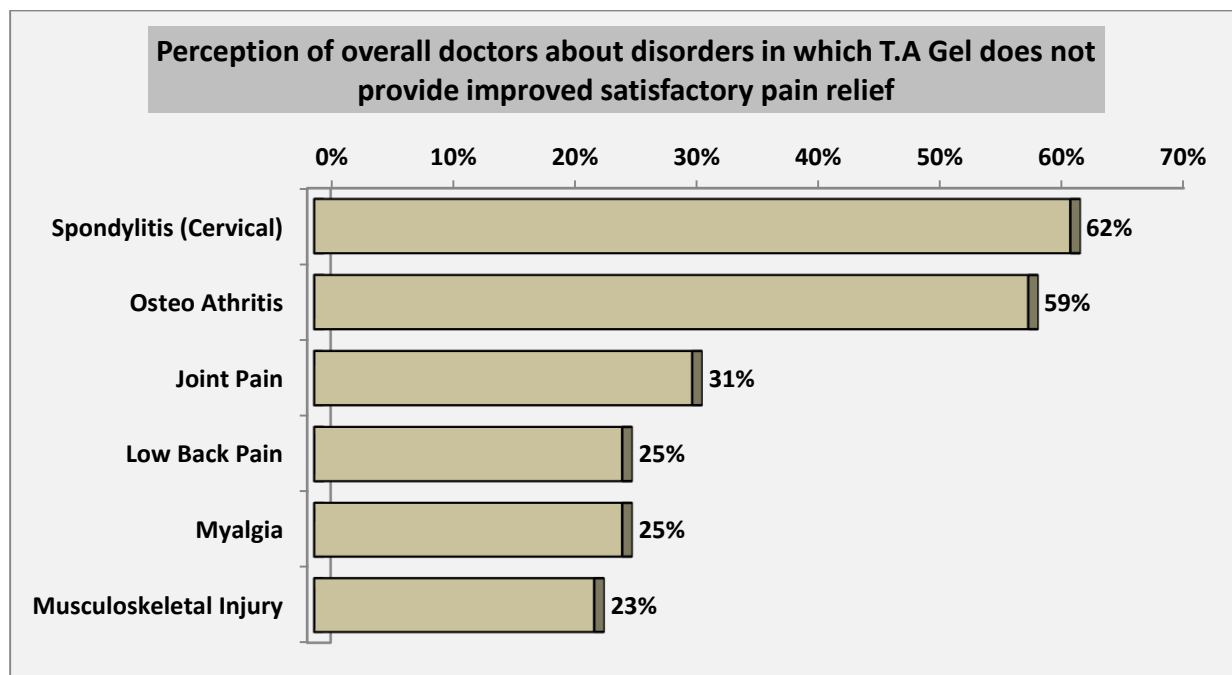
Q.5) Doctor, in what % of patients treated with Topical Anti-Inflammatory Gels will provide improved pain relief?



INTERPRETATION:

- ❖ Majority of overall doctors perceive that Topical Anti-Inflammatory & Analgesic Gels provide improved pain relief in only 50-60% patients.
- ❖ On Analyzing, 50% of overall doctors says that patients treated with Topical Anti-Inflammatory & Analgesic Gel will get <50-60% improved pain relief.
- ❖ Almost 79% of C.Ps perceives that <50-60% patients treated with T.A Gels will get an improved pain relief.
- ❖ Almost ~71% of G.Ps perceives that <50-60% patients treated with T.A Gels will get an improved pain relief.
- ❖ This implies that most of the doctors perceive that T.A Gels (recently available) does not provide significant pain relief in patients.

Q.6) Doctor, in which of the disorders you think that the recently available T.A. Gels does not provide satisfactory pain relief in patients?

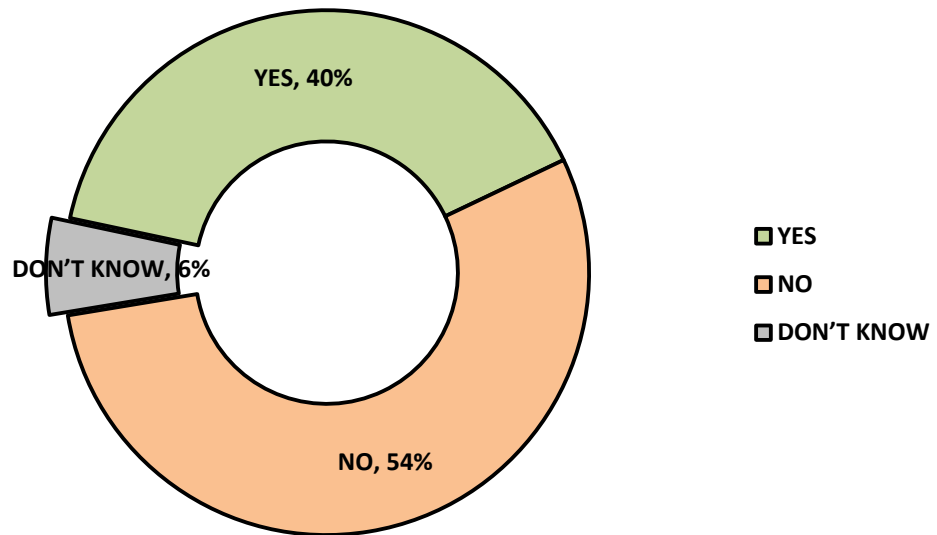


INTERPRETATION:

- ❖ Majority of overall doctors perceive that Topical Anti-Inflammatory & Analgesic gel does not gives satisfactory pain relief in Spondylitis cervical (62% of responded doctors) and Osteoarthritis (59% of responded doctors).
- ❖ It is followed by Joint Pain (31% of responded doctors) & Low Back Pain (25% of responded doctors).
- ❖ Only 23% (least) of the doctors perceive that Topical Anti-Inflammatory & Analgesic Gels doesnt give satisfactory pain relief in Musculoskeletal Injury.
- ❖ This implies, doctors perceive that T.A Gels does not give satisfactory pain relief in Severe and Chronic conditions of Pain.

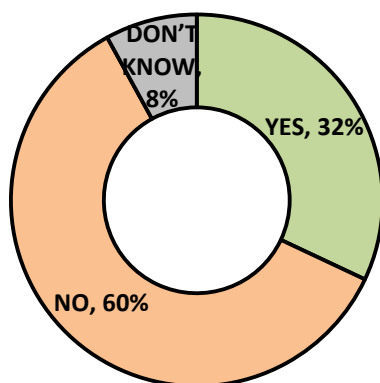
Q.7) Doctor, do you feel there is need for higher concentration of Diclofenac & combination Gel for better relief from pain?

**Overall Doctors need for higher concentration
Diclofenac & Comb. Gel**



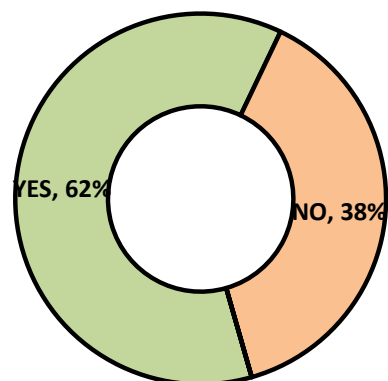
Need among G.P

■ YES ■ NO ■ DON'T KNOW



Need among C.P

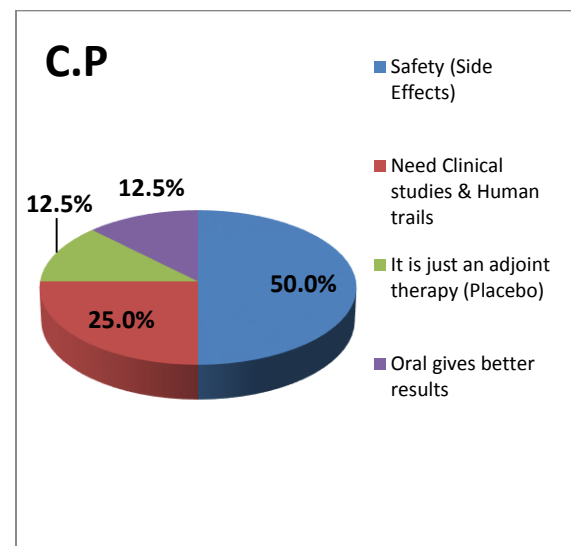
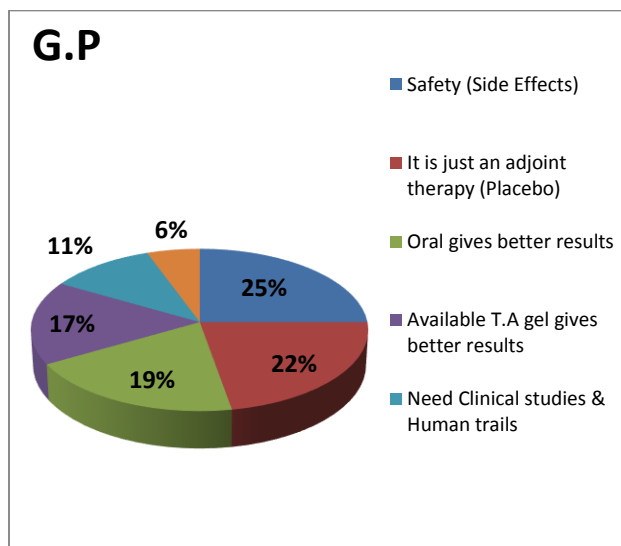
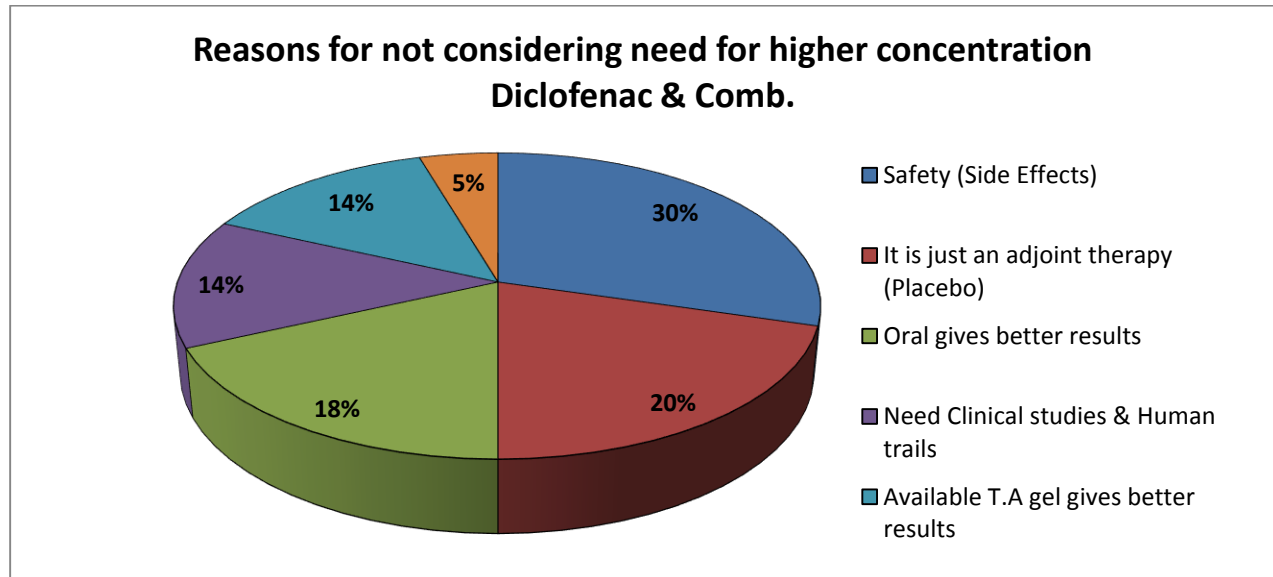
■ YES ■ NO ■ DON'T KNOW



INTERPRETATION:

- ❖ Majority of overall doctors (54%) consider that there is no need for higher concentration Diclofenac & Combination gel.
- ❖ Splitting the responses by speciality wise, highest percentage of G.Ps (60%) considers that there is no need for higher concentration Diclofenac & Combination gel.

Q.8) Doctor, is there any specific reason for not considering the need for higher concentration Diclofenac & Combination gel?



INTERPRETATION:

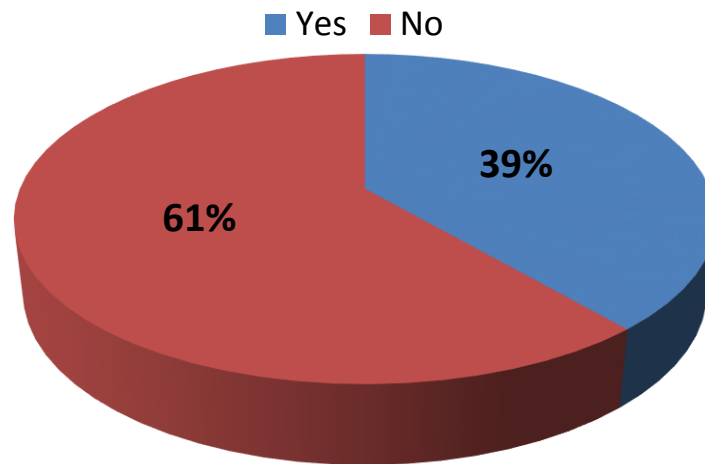
- ❖ The leading reason for not considering the need for higher concentration Diclofenac & Combination gel among the doctors is the concerns for “Safety (Side Effects)”
- ❖ Second most important reason for not considering need for higher concentration Diclofenac & Combination Gel is requirement of “Clinical

studies & Human trails” among C.Ps for justification of higher concentration Diclofenac & Combination gel.

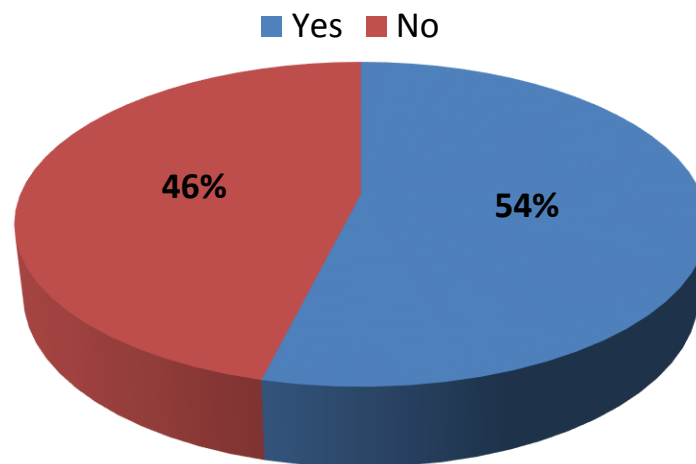
- ❖ G.Ps thinks that Topical Analgesic acts as a placebo, so they do not consider the need for higher concentration Diclofenac and Combination gel.

Q.9) Doctor, are you aware higher concentration of Topical Anti-Inflammatory & Analgesic Gels with 2% Diclofenac & combinationGel?

Awareness of 2% Diclofenac T.A Gel among G.Ps



Awareness of 2% Diclofenac T.A Gel among C.Ps



INTERPRETATION:

- ❖ C.Ps are more aware about about 2% Diclofenac T.A Gel than G.Ps
- ❖ 61% of General Physicians are not aware about 2% Diclofenac T.A Gel; this shows less penetration of 2% Diclofenac in market.

Q.9) Doctor, in which Indications do you think there is a need of higher concentration (2%) Diclofenac and combination Gel?

General Physician (G.P)		Consulting Physician (C.P)	
Rank	Indications	Rank	Indications
1	Severe Pain	1	Arthritis
2	Low Back Pain	2	Osteoarthritis
3	Arthritis	3	Low Back Pain
4	Osteoarthritis	4	Muscular Spasm
5	Sprain	5	Chronic Pain & Inflammation
6	Joint Pain	6	Joint Pain
7	Traumatic Injury	7	Inflammation
8	Muscular Spasm	8	Severe Pain
9	Chronic Pain & Inflammation	9	Traumatic Injury
10	Inflammation	10	Sprain

INTERPRETATION:

- ❖ G.Ps most preferred Indication for 2% Diclofenac is Severe Pain followed by Low Back Pain and Arthritis.
- ❖ C.Ps most preferred Indication for 2% Diclofenac is Arthritis, Osteoarthritis and Low Back Pain.

- ❖ This shows that G.Ps prefers 2% in Severe Pain in any part of musculoskeletal system, but C.Ps prefers more in chronic conditions.
- ❖ Low Back Pain is preferred by both specialties in their top three recommendations of indications.

5. Recommendations:

Marketing Strategy:

Market Segmentation-

1) Identify Bases for segmenting the Market:

General Physician and Consulting Physicians together contribute to 34% of prescription share contributing to 1/3rd of the prescription share of Topical NSAIDs. 9.7% of Rx and 9.9% Rx generated by G.Ps and C.Ps respectively in Topical NSAIDs contributes to Volini, which is highest among all brands. (SMSRC Rx data)

2) Profiles of Resulting Segment:

- General Physicians (G.Ps)
- Consulting Physicians (C.Ps)

Market Targeting-

1) Measures of Segment Attractiveness-

General Physician and Consulting Physician according to the findings (Primary Research) treats 7 MSD (62% of them are prescribed with Topical Analgesic Gel) patients and 6-7 MSD (67% of them are prescribed with Topical Analgesic Gel) patients per day respectively and SMSRC Rx data shows that G.P + C.P together contributes to the one third (1/3) of the total prescription of topical NSAID

Target Segment (Consumers):

- Anyone suffering from:
 - Back, knee and neck pains
 - Internal pains & strains,
 - Sports related injuries and other musculoskeletal injury
 - Chronic conditions like Arthritis, Spondylitis and Osteoarthritis etc.

Group	Needs
Old age segments	Joint pains & ageing
Sports persons	Sports related injuries
Transport	Work/stress related
Desk jobs	Work/stress related
Homes with housewives	Relief from recurring back pains, joint pains and more.

Market Mix for each target segment:

Product: Novelty factor for product is 2% Diclofenac in Topical Anti-Inflammatory and Analgesic Gel for faster, better and long lasting relief.

Price: Value based pricing (Providing quality product at fair price) should be considered or Competitive pricing, because G.Ps and C.Ps are more sensitive towards change in price (So premium price cannot be kept).

Competitor details with Pricing:

Brand (Formulation)	MS(%) MAT Feb-'16	Composition	Price (Rs/SKU)
Voveran (Gel)	8.8%	DDEA - 1.16%w/w	86.75/ 30gm
D.F.O (Gel)	4.7%	DDEA – 1.16%w/w MS – 10% Menthol – 5%	79/ 30gm
Oxalgin (Gel)	4.7%	Diclofenac – 1%w/w Menthol – 50mg/1G MS – 150mg	90/ 30gm
Dynapar QPS (Solution)	3.5%	DDEA – 4.64%w/v Abs.Alcohol – 10%	197 / 30ml
Nobel (Gel)	2.8%	DDEA – 1.16%w/w Linseed Oil – 3%w/w MS – 10% Menthol – 5%	55/ 30gm 22/ 10gm

Promotion:

For promotion separate promotion strategy and Promotogram has to set up for both G.Ps and C.Ps because according to the findings of the Primary Research, the need and awareness for 2% Diclofenac T.A Gel is different for both the specialties.

General Physicians: (G.Ps)

The need is less among G.Ps and awareness is also less, thus for first six months awareness has to be created for 2% Diclofenac T.A Gel and the product has to be backed by Clinical support, so Clinical articles and studies has to be distributed for safety and efficacy for 2% Diclofenac in T.A Gel (As safety was the important reason for not considering the need for 2% Diclofenac among G.Ps).

Initially samples can to be distributed for demonstration and efficacy of product, which will help is defining and refining the strategies more clearly.

Campaigns for Musculoskeletal Disorder awareness can be run along with CME (Continuous Medical Education) for 2% Diclofenac and its benefits among doctors.

G.Ps has to be promoted the 2% Diclofenac T.A Gel for Severe Pain and more of Low back pain, Joint Pain, Neck & Shoulder Pain along with some chronic conditions (e.g. Arthritis).

Consulting Physicians: (C.Ps)

54% of C.Ps according to study are aware, but still lot of them are not aware, hence awareness should be created for 2% Diclofenac T.A Gel.

Clinical Studies and articles have to be distributed among C.Ps for providing the evidence based support for 2% Diclofenac T.A Gel.

Volini brand loyal customers have to be focused initially and then slow penetration can be done into untapped arena.

Campaigns for Musculoskeletal Disorder awareness can be run along with CME (Continuous Medical Education) for 2% Diclofenac and its benefits among doctors.

C.Ps has to be promoted the 2% Diclofenac T.A. Gel for Chronic conditions and Acute conditions both (e.g. Low back pain, Arthritis, Joint Pain etc)

Positioning:

2% Diclofenac Topical Anti-Inflammatory and Analgesic Gel should be position as the powerful, deeper, faster and long lasting relief from Musculoskeletal Pain, Injury and Inflammation. It can also be position as a new product with stronger and double strength Diclofenac as an Active Pharmaceutical Ingredients (API).

6. Clinical Studies and Human Trails:

(Evidence based support for new product 2% Diclofenac gel)

CLINICAL STUDIES & HUMAN TRAILS			
Study Title/ References	Attributes considered	Methodology (Study Characteristics)	Results/Conclusions
Topical Analgesics in the management of acute and chronic pain Argoff; CE. (2013)	Acute and Chronic Pain	A literature search of MEDLINE/PubMed was conducted focused only on individual clinical trials published in English-Language journals. The search identifies 92 articles, of which 65 were eligible for inclusion in the review.	Strong evidence was identified for the use of topical diclofenac and topical ibuprofen in the treatment of acute soft tissue injuries or chronic joint-related conditions, such as osteoarthritis.
Topical Non-steroidal anti-inflammatory drugs for acute musculoskeletal pain in adults Derry S, et al (2015)	Acute musculoskeletal disorders like strains, sprains and overuse injuries	A review including the randomized, double-blind, active or placebo (inert carrier)_controlled trials in which treatments were administered to adults with acute pain resulting from strain, sprains or aports or overuse- type injuries (twisted ankle). They identified 14 studies to add to 47 studies included in the earlier review. The 61 studies involving 8386 participants were generally of high quality. They tested a number of different topical drugs, mostly against a topical placebo, with application atleast once a day. Outcome measure: Pain reduction by Half around seven days after treatment started.	Topical NSAIDs provided good levels of pain relief in acute conditions such as sprains, strains and overuse injuries, probably similar to that provided by oral NSAIDs. Adverse events were usually minimal. Gel formulation of diclofenac and ketoprofen were among the most effective, along with ibuprofen gel and diclofenac plaster.
Topical NSAIDs for chronic musculoskeletal pain in adults Derry S et al (2015)	<u>Chronic Musculoskeletal Conditions:</u> Knee Arthritis, Osteoarthritis and other severe or moderate intensity etc	The review is an update of Topical NSAIDs for chronic musculoskeletal pain in adults. 39 high quality studies with 10631 participants where topical NSAIDs used at least once a day were included. Tests were compared mostly with placebo. Authors were interested in participants with good pain reduction, ideally 6 to 12 weeks after the treatment. Individual NSAIDs were looked for their effectiveness	Diclofenac & Ketoprofen were the two with good quality longer duration studies, mostly in people over 40 years of age. For Diclofenac & Ketoprofen, about 6 people out of 10 with osteoarthritis had much reduced pain after 6 to 12 weeks compared with placebo. Skin reactions were common with topical Diclofenac (20/100) than placebo. Serious adverse events were uncommon.
Topical Therapy in Management of Chronic Pain Stanos SP et al (2013)	- Chronic soft Tissue Pain - Osteoarthritis - Chronic musculoskeletal & Neuropathic pain	Review of the Past and Currently available Articles	Data suggest that topical therapies may offer a safe, well-tolerated, and effective alternative to systemic therapies in the treatment of patients with chronic, localized musculoskeletal and neuropathic pain

Safety profile of topical diclofenac: a meta-analysis of blinded, randomized, controlled trials in musculoskeletal conditions Taylor RS (2011) CMRO	Safety and Tolerability of Topical Diclofenac	To evaluate the risk of adverse events (AEs) associated with topical diclofenac for the treatment of acute and chronic musculoskeletal conditions. Systematic review and meta-analysis of blinded, randomized, placebo-, vehicle- or active-controlled trials.	Conclusion: Topical diclofenac appears to be generally well tolerated for cutaneous use in acute and chronic musculoskeletal conditions
A comparison of the pharmacokinetics and tolerability of diclofenac sodium 2% and 1.5% topical solutions R. Franke et al (Journal of Pain)	Pharmacokinetics and Tolerability of Diclofenac 2% & 1.5% topical solutions	Two similar cross over study (RCT) characterized the pharmacokinetics and tolerability of diclofenac sodium 2% solution in relation to diclofenac 1.5% topical solution	Diclofenac 2% solution has higher Diclofenac plasma concentration than 1.5% solution. Mild application site reactions (i.e, dryness, erythema and pruritis) were most common. Substantially lower systemic exposure of topical application relative to oral dosage form.
AB0863 Systemic Bioavailability of Diclofenac Diethylamine 2.32% Gel Versus Oral Diclofenac Sodium Tablets (50 MG) in Healthy Volunteers: A Randomized, Open-Label, Crossover Study M. Armogida et al, 2015 (Annals of Rheumatic disease) The Eulars journal	To compare the systemic bioavailability of diclofenac following topical application of DDEA 2.32% gel (4 g per knee, twice per day) on 1 knee vs. 2 knees, and vs. oral diclofenac sodium (50 mg tablet, three times per day) in healthy volunteers representative of the OA population	In this open-label, crossover, systemic bioavailability study, 40 healthy volunteers (mean age 60 years) were enrolled to receive all three above mentioned treatments for 7 days in a randomized sequence. Pharmacokinetic data in plasma and urine and safety data were collected throughout. The study was completed by 35 subjects and data from 38 subjects was included in the analysis	Systemic exposure to diclofenac from either topical regimen was very low. Twice-daily application of DDEA 2.32% gel to 2 knees for 7 days roughly doubled systemic exposure vs. application to 1 knee. Oral dosing with diclofenac sodium tablets (50 mg, three times daily) increased systemic exposure on Day 7 vs. topical dosing by 1–2 orders of magnitude. Local and systemic tolerability of topical DDEA gel were excellent.
Efficacy and safety of diclofenac sodium 2% topical solution for osteoarthritis of the knee: a randomized, double-blind, vehicle-controlled, 4 week study Wadsworth LT et al (2016)	Osteoarthritis of knee (Pain)	Study type: A phase II, 4week, double blind Randomized controlled trail. Number of subjects: 260 Patient's age: 40-85 years	Results: Of 260 patients randomized, 259 received ≥ 1 dose of study drug. Significantly greater reductions in least-squares mean (standard error) WOMAC pain scores were observed for diclofenac-treated (-4.4 [0.4]) versus vehicle-treated patients (-3.4 [0.4]) at the final visit ($p = 0.040$). The most commonly reported TEAEs were administration site conditions. The vehicle-treated group experienced slightly more TEAEs than the active treatment group (38.8% vs. 31.5%). No serious adverse events were reported. Conclusion: Administration of diclofenac sodium 2% topical solution BID resulted in significantly greater improvement in pain

			reduction in patients with OA of the knee versus vehicle control and was generally well tolerated.
An assessment of the efficacy and tolerability of diclofenac sodium 2% topical solution for treating osteoarthritis of knee T.Barrett et al (Journal of Pain)	Osteoarthritis of knee (Pain)	Study type: Double-blind, randomized, controlled, parallel-group study assessed the efficacy and tolerability of Diclofenac 2% topical solution in O.A patients. Patients were randomly assigned to receive Diclo.Na 2% topical solution or vehicle applied twice daily for 4 weeks.	Regardless of missing data imputation method used, diclofenac sodium 2% topical solution using twice daily dosing regimen produced significantly greater improvements in pain reduction associated with osteoarthritis of the knee compared to vehicle control and was generally well tolerated. Supported by funding from Mallinckrodt Inc.
Efficacy and Safety of Diclofenac Diethylamine 2.32% Gel in Acute Ankle Sprain (Two applications per day (morning and evening) suffice to exert a therapeutic effect that could last for up to 12 h.) HANS-GEORG PREDEL et al	Acute Ankle Sprain	This randomized double-blind controlled study enrolled patients with acute ankle sprain treated with DDEA 2.32% gel two times per day (bid) (n = 80) or three times per day (tid) (n = 80) or placebo (n = 82). Efficacy (including pain and swelling) and local tolerability were evaluated during 8 T 1d.	Topical diclofenac diethylamine (DDEA) 2.32% gel achieves lasting efficacy in localized pain with two applications per day, while maintaining the favorable safety profile of topical diclofenac and potentially improving convenience and patient compliance Conclusion: DDEA 2.32% gel twice daily (applied in the morning and evening) was well tolerated and provided lasting relief from pain, improved function, and reduced symptomatic healing time in uncomplicated ankle sprain.
Comparison Between Two Diclofenac Diethylamine Gel Formulations, 1.16% Vs 2.32%: Is It Only Increasing the Strength of the Active Ingredient Enough? Giuseppa Quartarone et al (American College of Rheumatology)	Penetration & Permeation of Diclofenac with PE (Penetration Enhancer)	Methods: In vitro skin penetration studies were performed at 35°C in glass Franz static diffusion cells using human skin. Samples of donor abdomens were obtained from the NDRI Institute (USA) and the WHRTB Institute (HU) and kept frozen at -80°C until use. The comparison of in vitro skin permeation of VEG 1% vs VEG 2% was performed. Then VEG 1% was tested against VEG 2% containing low (0.5%), medium (0.75%) and high (1.0%) amounts of a permeation enhancer. All samples were applied at 20 mg/cm ² in a single dose, equivalent to the maximum daily dose of 4 applications of 5 mg/cm ² under in use conditions.	Results: Addition of the PE at the VEG 2% gel resulted at a dose-dependent (up to 3-fold) increase in diclofenac's skin permeation (Fig. 1). Medium and high PE concentration resulted in similar cumulative permeation. Conclusion: Addition of PE to VEG 2% resulted in an up to 3-fold increased diclofenac skin permeation which correlated with the PE dose concentrations. The new gel is expected to have a lasting effect, e.g. up to 12h, potentially attributed to the release of a higher amount of drug at the application site as confirmed in a RCT (Predel 2012), where 2 daily doses significantly reduced pain and improved joint function vs placebo. This could be useful when treating flares of peripheral joint conditions such as OA.

Overview of the safety of diclofenac diethylamine 2.32% gel Huskisson ED et al (2011)	Acute Ankle sprain, Adverse events (AEs) Safety of 2.32% DDA gel	AEs reported in: Two randomized, double-blind, placebo-controlled trials in patients with acute ankle sprain (n=513). Patients were treated with DDEA 2.32%gel od(n=91),bid (n=169) or tid (n=80), placebo (n=173).	DDEA 2.32% gel is well tolerated Low incidence (0.6%) of drug related AEs at the application site in RCT in Acute ankle pain No drug related AEs at the application site with DDEA 2.32% gel in P'kinetic and local tolerability trials in healthy volunteers. Topical treatment with DDEA 2.32% gel was well tolerated locally, even under occlusive conditions, with few drug-related local adverse effects that were mostly mild to moderate. The phototoxic potential with DDEA 2.32% gel was minimal.
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7. Questionnaire:

Questionnaire for Doctors

CONSENT:

Doctor, I Adil Refai student of IIHMR University-Jaipur. As a part of my curriculum I am working on a project and with your permission, I would like to understand your perception and preferences for Topical Anti-Inflammatory & Analgesic Gel.

Date: _____

Respondent details:

Specialty	:
Name	:

Gender	:	(M)	(F)
Address (Area)	:		

Q.1) Doctor, what are the numbers of patients of Musculoskeletal Disorders (e.g. Low back pain/Joint pain/Arthritis and related disorders) do you treat per day?

Q.2) Doctor, Out of the above number of patients treated how many patients do you prescribe Topical Analgesic Gel?

Q.3) Doctor, which molecules you prefer in Topical Analgesic Gel:

Molecule	Dose (No of application of Gel/day)	Duration of therapy (days)

Q.4) Doctor, which are the top three Topical Analgesic gel brands that you prescribes?

1) _____ 2) _____ 3) _____

Q.5) Doctor, in what % (Out of 100) of patients treated with Topical Anti-Inflammatory & Analgesic Gel, showed the following results?

- Improved pain relief: _____ % of patient out of 100%

Q.6) Doctor, please tick mark (✓) in given box, the disorder/disorders in which you think that the recently available Topical Anti-Inflammatory & Analgesic gels does not provide satisfactory pain relief.

Please tick mark (✓) your preferred opinion in the given box:

Tick Mark(✓)	Disorders
	Low back pain
	Joint pain
	Musculoskeletal injury
	Osteoarthritis Knee
	Myalgia
	Spondylitis (Cervical)

Q.7) Doctor, do you feel there is need for higher concentration of Diclofenac & combination Gel for better relief from pain?

a) Yes

b) No

c) Don't Know

If response is "No" in Q.7,

Q.8) Doctor, is there any specific reason for not considering need for higher concentration of Diclofenac & combination gel?

Q.9) Doctor, are you aware about higher concentration of Topical Anti-Inflammatory & Analgesic Gels with 2% Diclofenac & combination Gel?

a) Yes

b) No

Q.10) Doctor, in which Indications do you think there is a need of higher concentration (2%) Diclofenac & combination Gel?

"Thank you so much Doctor for your Valuable participation"

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9. Summer Internship Activity Plan:

SUMMER INTERNSHIP ACTIVITY PLAN								
ACTIVITY	April				May			
	4 TH APRIL TO 7 TH APRIL	8 TH APRIL TO 15 TH APRIL	16 TH APRIL TO 22 ND APRIL	23 RD APRIL TO 30 TH APRIL	1 ST MAY TO 7 TH MAY	8 TH MAY TO 15 TH MAY	16 TH MAY TO 22 ND MAY	23 RD MAY TO 31 ST MAY
Literature review and Desk research (IMS Data & SMSRC Data)								
Submission of Executive summary of Desk research & Preparation of Questionnaire								
Pilot study & Questionnaire refining								
Field work (Primary data collection)								
Data segregation and Analysis and Report writing								
Presentation and Final Report submission								