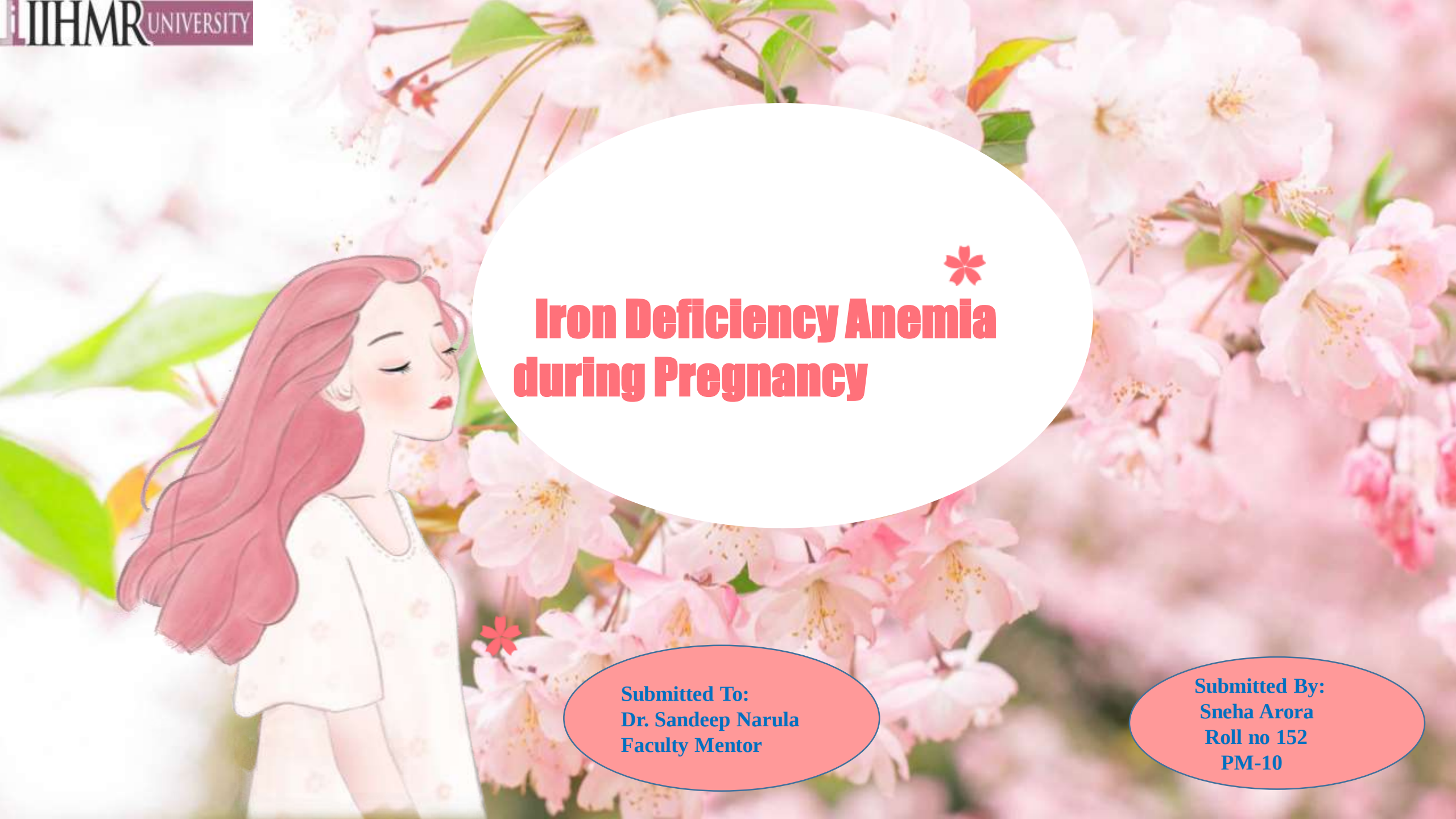




Iron Deficiency Anemia during Pregnancy

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Roll no 152
PM-10**

Introduction

- **Iron deficiency anemia (IDA)**- Anemia due to iron deficiency is common sort of anemia , occurs when an individual's iron supply is lower than the physiological amount required it leads to decrease in number of red blood cells (RBC) or hemoglobin.
- In this red cells appear microcytic and hypochromic
- The normal diet contains 15-20 mg of iron, and the body absorbs only 1-2 mg/d of dietary iron.
- Iron is essential for cell metabolism and growth, and is distributed between 3 compartments in the cell: the transit pool, the storage pool, and the functional pool.

IDA During Pregnancy

- Pregnant women are more susceptible to IDA, as their need for iron increases to three times.
- During the pregnancy ,Hb concentration <11 g/dL in the first trimester or <10 g/dL in the second and third trimesters.
- According to WHO prevalence of Iron deficiency in India is 53.0% in 2015–2016 Prevalence of anemia in pregnant women in India is determined 50 % in NFHS survey (2015-16)
- India 70% of maternal deaths occur due to anemia, out of which 20% maternal deaths are directly due to anemia
- Daily need of is approximately 27 milligram during pregnancy and 1gm during whole pregnancy.

Cont:

Iron demands increase during Pregnancy

- During pregnancy, physiologic iron demands increase substantially to support fetoplacental development and maternal adaptation to pregnancy.
- Fetoplacental unit requires a large amount of iron for its own growth and development during gestation
- Expansion in plasma , Hb mass and blood volumes to maintain proper circulation and oxygen
- Delivery to her own organs as well as to the placenta

Iron demand in each trimester

During pregnancy, iron requirements are not uniform

- **First trimester**-daily needs decrease due to the absence of menstruation. This represents a saving of approximately 0.56 mg of iron per day but losses from the gut, skin and urine approximately 14 µg/kg/day
- **Second trimester**- blood volume increases by 45%, with an increase in plasma volume of 50%; red cell mass is raised by 35% in iron-replete women. This requires approximately 450 mg of iron .
- **Third trimester**-Fetal demands for iron are maximal during the third trimester. The iron content of a 3 kg fetus has been estimated at 270 mg.

Iron Absorption and Transportation

➤ **Iron Absorption-** Iron is absorbed in the duodenum and upper jejunum, when iron passes through a membrane of cells called enterocytes that line the intestine.

➤ **Iron transport and usage**

Iron from intestinal mucosal cells is transferred to transferrin (transferrin is a glycoprotein, synthesized in the liver) iron is transferred from enterocytes into the plasma. Fe^{2+} ion transport it outside the cell in systemic circulation from (transmembrane protein) ferroportin

Iron later passes to bone marrow, where it is used to make hemoglobin and red blood cells, which circulate in body and helps in supplying oxygen to organs and tissues.

Synthesis of transferrin increases with iron deficiency but decreases with any type of chronic disease.

Iron Storage and Recycling

Iron not used for erythropoiesis is transferred by transferrin to the storage pool

- **Ferritin** (a heterogeneous group of proteins surrounding an iron core)- soluble and active storage fraction located in the liver (in hepatocytes), bone marrow, and spleen (in macrophages); in red blood cells (RBCs); and in serum.
- **Hemosiderin**- insoluble and is stored primarily in the liver (in Kupffer cells) and in the bone marrow (in macrophages).
- **Recycling of iron** - Transferrin grasps and recycles available iron from aging RBCs undergoing phagocytosis by mononuclear phagocytes.

Iron Homeostasis

Excess iron stored within hepatocytes.

- Hormone hepcidin released from liver regulates systemic iron balance by regulating ferroportin concentration on iron exporting cells to inhibit iron absorption from the duodenum and iron release from macrophage and hepatocyte stores.
- High hepcidin block intestinal iron absorption And macrophage iron recycling , causing iron restricted erythropoiesis and anemia.
- Inflammation stimulates hepcidin production, Consequently, at the cellular level, iron overload in the host cells including enterocytes and macrophages is established, while at the systemic level, iron deficiency (ID), ID anemia (IDA) and anemia of inflammation (AI) have been found.

Changes in hepcidin during Pregnancy

In high-risk pregnancies – associated with inflammatory processes, obesity, Gestational Diabetes and preeclampsia, higher hepcidin levels in serum compared to healthy controls have been found.

Elevated hepcidin levels during pregnancy might cause iron restriction of mother and insufficient placental iron supply to the foetus.

Increase in concentration of hepcidin lead to “Functional iron deficiency”- relative ID in blood resulting from excess storage of iron in the form of ferritin, i.e. in the presence of adequate iron stores.

In hepcidin excess resulting from inflammation, iron absorption from supplemental sources is markedly decreased and iron supplementation has no benefit.

Current IDA Management Therapy

- ❖ Oral iron therapy
- ❖ IV iron therapy
- ❖ RBC Transfusion
- ❖ Erythropoiesis-Stimulating agents

Limitations of Current Therapy

Oral iron

- Poor absorption
- GI Side effects
- Dyspepsia, nausea, vomiting, abdominal pain, constipation or diarrhoea, due to the oxidative properties of iron on the intestinal mucosa.
- Dose dependent GI side effects affect compliance.
- Pro-oxidant effect leads to staining of mucous and stools.

IV iron

- Iron overload and tissue damage
- increase in non-transferrin bound iron (NTBI)
- Risk of infection
- Increases oxidative stress
- Painful to the patients
- Poor compliance

Lactoferrin

- ❖ Lactoferrin is a new generation oral iron that has long been recognized as a member of the transferrin family of proteins
- ❖ Lactoferrin differs from transferrin by its higher affinity for iron is 300 times greater and its ability to retain iron at a pH lower than 4 such as exist in the gastrointestinal tract.
- ❖ Lactoferrin was found not only in milk and in human colostrums, but also in other external secretions with lower concentration, such as saliva, tears, semen, and mucosal secretions, and as an important constituent of the neutrophilic granules of leucocytes.
- ❖ It is involved in several physiological functions, including: regulation of iron absorption in the bowel; immune response; antioxidant, anticarcinogenic and anti-inflammatory properties; and protection against microbial infection.

Mechanism of action

Lactoferrin mainly works in 4 ways:

1. By Regulating Hepcidin Ferroportin Axis
2. By Downregulating Inflammation
3. By Increasing Compliance
4. Increase in Systemic Iron Reserve

Unmet need and future up gradation required

1. Tablets which have high absorption rate in low pH .
2. Oral liposomal iron
3. Controlled release tablets
4. Combinations with other micronutrients
5. Quality and packaging of iron supplement
6. Cost of therapy

Competitor IDA Analysis:

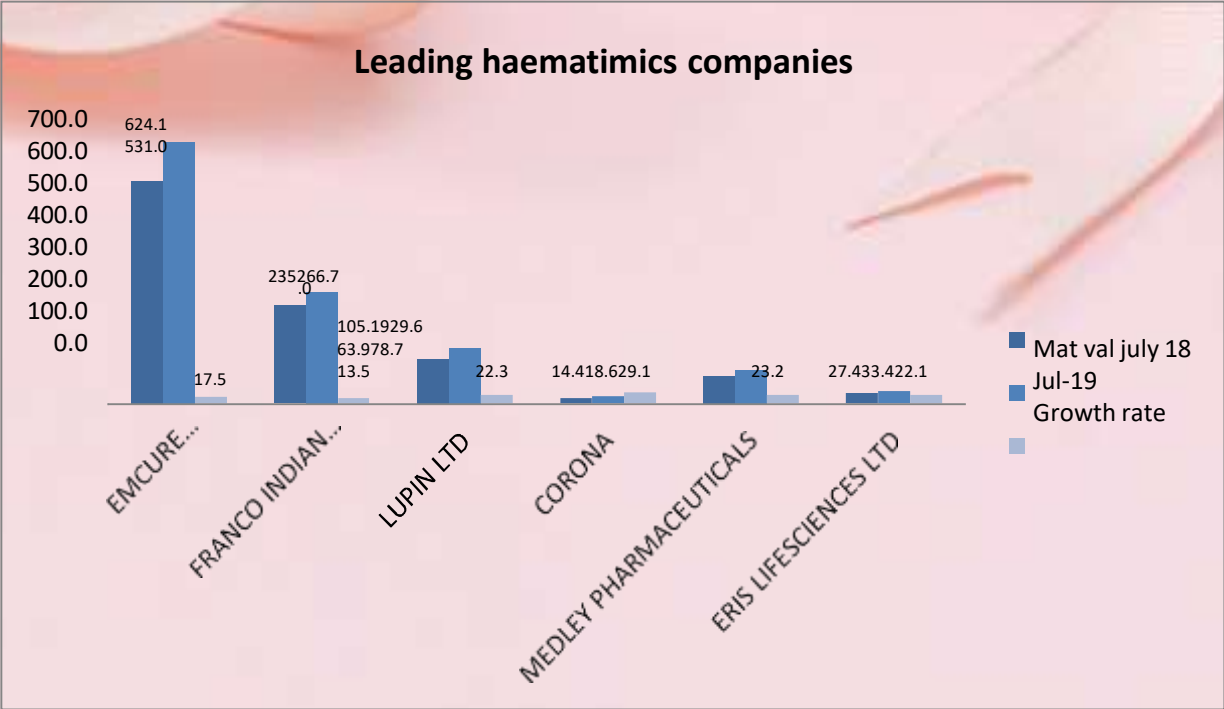
The moving annual turnover of Indian Haematinics market 2019 was estimated

21.562 billions (MAT 19- 2156.2 cr) with the Growth Rate of approx **10.1 %**. Previously in 20018 the MAT was **19.586 billion** (1958.6 cr).

Competitive profiling analysis is done with companies like Emcure, lupin, Franco Indian pharmaceuticals, Zuventus healthcare ltd., Medley pharmaceuticals, Alkem laboratories, Macleods pharmaceuticals, Aristo pharmaceuticals, Indchemie health specialist.

Data of MAT value 18, MAT value 19 and GR is used to analyze the product with with high MAT value and GR and for understanding leading IDA molecules of competitor profile.

List of top 6 corporate according to their MAT values are given below:

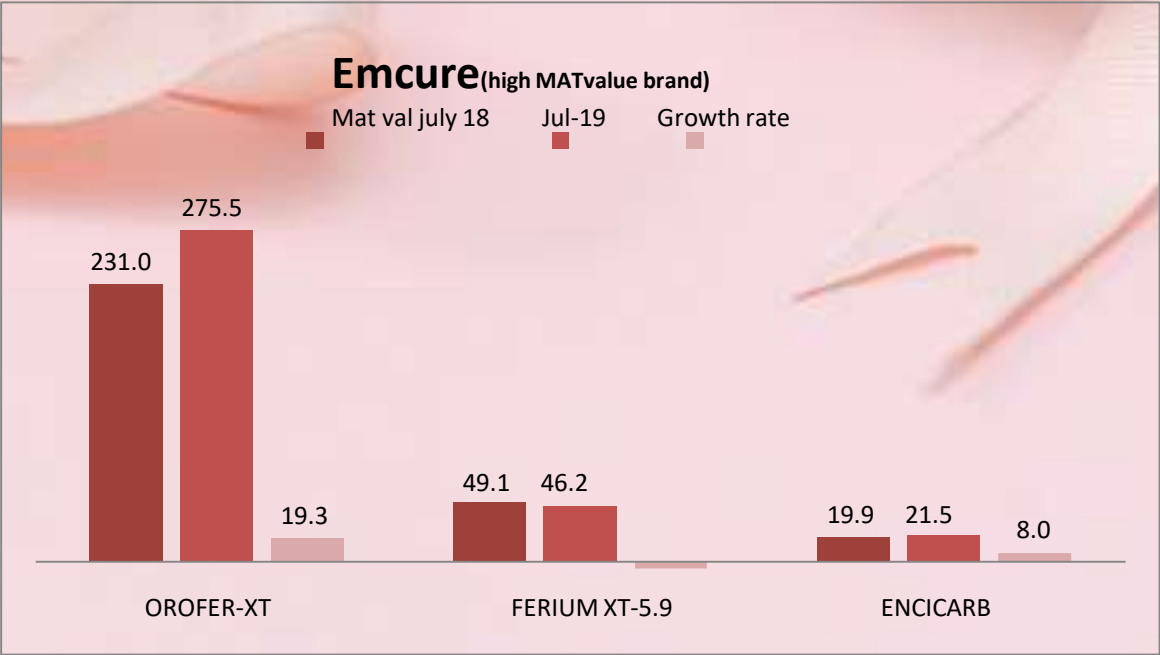


Company	Mat val july 18	MAT Jul-19	Growth rate
EMCURE PHARMACEUTICALS LTD	531.0	624.1	17.5
FRANCO INDIAN PHARMACEUTICALS PVT LTD	235.0	266.7	13.5
LUPIN LTD	105.9	129.6	22.3
CORONA	14.4	18.6	29.1
MEDLEY PHARMACEUTICALS	63.9	78.7	23.2
ERIS LIFESCIENCES LTD	27.4	33.4	22.1

ANALYSIS:

The Six(6) corporate Emucure pharmaceuticals showed the highest Growth Rate of 17.5% with the MAT19 value (624.1 cr).

Data of top brands of individual company is given below



Brand	Mat val july 18	Jul-19	Growth rate
OROFER-XT	231.0	275.5	19.3
FERIUM XT	49.1	46.2	-5.9
ENCICARB	19.9	21.5	8.0

list of top 3 brands of Emcure with high MAT value

ANALYSIS:

•Emcure is the leading company of Haematinics of having MAT 19 value 624.1 cr and 17.5 % Growth rate.

Emcure OROFER- XT is the brand which showed highest MAT value (27.5 cr),

OROFER-XT is the extension of OROFER , other extension of OROFER are OROFER-FCM (121.3 cr),

OROFER-S (88.4 cr)

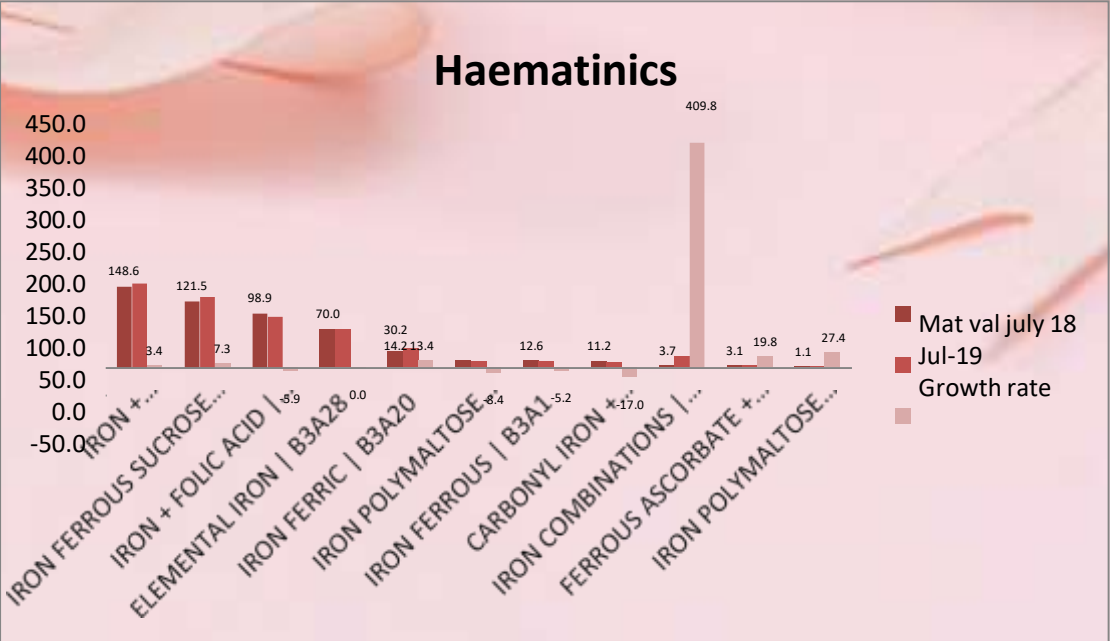
List of brands of Emcure with high Growth rate is given below

Brand	Mat val july 18	Jul- 19	Growth rate
FERIUM XT PLUS	0.0	4.1	40019.6
FERIUM 1K	5.8	13.5	131.6
COBAFORTE CD3	3.0	3.9	30.1

ANALYSIS:

Emcure FERIUM- XT plus brand showed highest Growth rate 40019% followed better the FERRIUM 1K with 131.6%, these are the extended brands of FERIUM

Data of leading molecules of haematinics are given below:

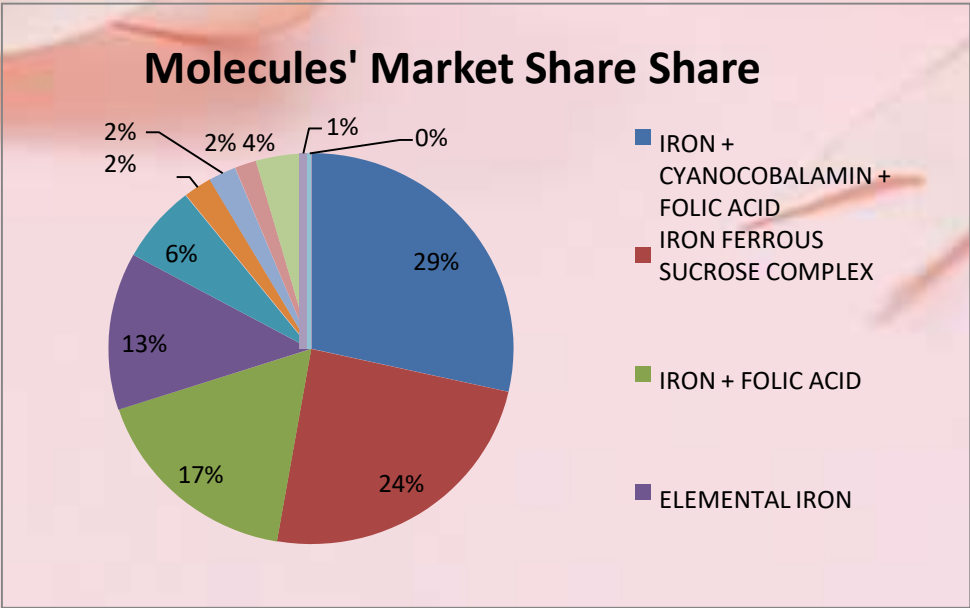


Sub super group	super group	Mat val july 18	Jul-19	Growth rate
HAEMATINICS	IRON + CYANOCOBALAMIN + FOLIC ACID	148.6	153.7	3.4
	IRON FERROUS SUCROSE COMPLEX B3A23	121.5	130.3	7.3
	IRON + FOLIC ACID B3A26	98.9	93.0	-5.9
	ELEMENTAL IRON B3A28	70.0	70.0	0.0
	IRON FERRIC B3A20	30.2	34.5	14.2
	IRON POLYMALTOSE COMPLEX B3A10	13.4	12.3	-8.4
	IRON FERROUS B3A1	12.6	11.9	-5.2
	CARBONYL IRON + OTHER COMBINATION B3A6	11.2	9.3	-17.0
	IRON COMBINATIONS B3A33	3.7	18.7	409.8
	FERROUS ASCORBATE + IRON + FOLIC ACID B3A17	3.1	3.7	19.8
	IRON POLYMALTOSE COMPLEX + ZINC B3A11	1.1	1.4	27.4
HAEMATINICS Total		514.3	538.8	4.8

ANALYSIS:

Iron + cynocobalamine + folic acid is a combination showed highest Mat 19 value (153.7 cr) with the Growth rate of 3.4 %, followed by iron ferrous sucrose complex with the MAT 19 value (130.3 cr) and Growth rate 7.3 %. Iron combination showed highest Growth Rate 409.8%

Molecule wise Market Share data



Molecule	MS (%)
IRON + CYANOCOBALAMIN + FOLIC ACID	28.5
IRON FERROUS SUCROSE COMPLEX	24.2
IRON + FOLIC ACID	17.3
ELEMENTAL IRON	13.0
IRON FERRIC	6.4
IRON POLYMALTOSE COMPLEX	2.3
IRON FERROUS	2.2
CARBONYL IRON + OTHER COMBINATION	1.7
IRON COMBINATIONS	3.5
FERROUS ASCORBATE + IRON + FOLIC ACID	0.7
IRON POLYMALTOSE COMPLEX + ZINC	0.3

ANALYSIS:

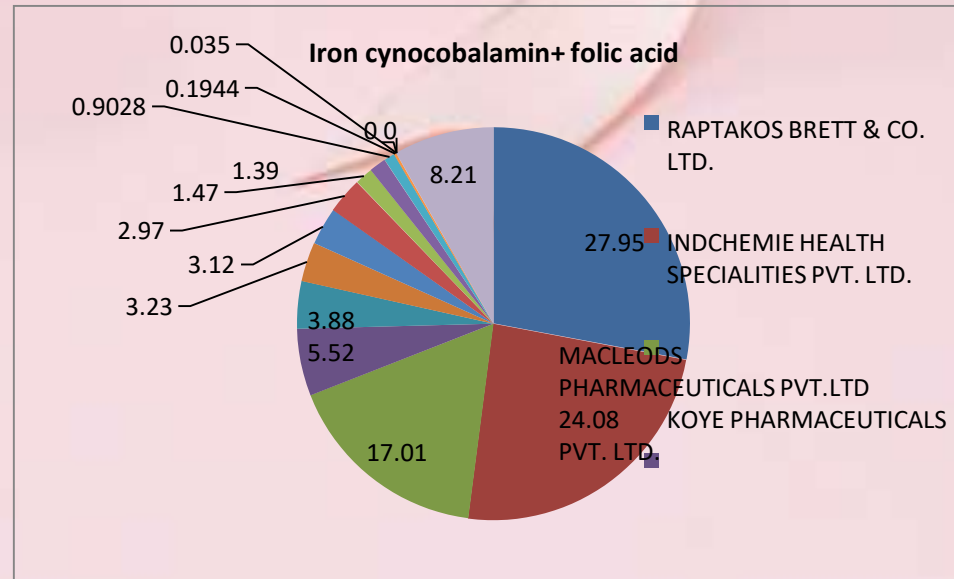
Amongst 11 molecules of haematinics combination of Iron cynocobalamin and folic acid is a leading molecule with market share of 29%

Company Wise Market Share of Leading Molecules

1. iron cynocobalamin and folic acid

IRON + CYANOCOBAL AMIN + FOLIC ACID / Brands	Company	MAT July'18 Val in Crs.	MAT July'19 Val in Crs.	MS (%)	GR (%)	Value Additio n in a year
		148.6	153.7	100.0	3.4	5.1
HEPATOGLOBIN	RAPTAKOS BRETT & CO. LTD.	41.1	43.0	27.9	4.6	1.9
CHERI	INDCHEMIE HEALTH SPECIALITIES PVT. LT	36.6	37.0	24.1	1.0	0.4
RUBIRED	MACLEODS PHARMACEUTICALS PVT.LTD	25.8	26.1	17.0	1.4	0.4
COEHB	KOYE PHARMACEUTICALS PVT. LTD.	9.3	8.5	5.5	-8.6	-0.8
IMFERON	SHREYA LIFE SCIENCES PVT. LTD	3.9	6.0	3.9	53.5	2.1
IREX	MICRO LABS LTD	4.3	5.0	3.2	15.6	0.7
MASHYNE	USV PVT LTD	6.2	4.8	3.1	-22.4	-1.4
FEROZORB	MACLEODS PHARMACEUTICALS PVT.LTD	4.8	4.6	3.0	-4.4	-0.2
HAEMADAY	AKUMENTIS HEALTHCARE LTD	1.7	2.3	1.5	35.6	0.6
I-FAG	AKUMENTIS HEALTHCARE LTD	3.4	2.1	1.4	-36.2	-1.2
RICHAR	ALEMBIC LTD	1.1	1.4	0.9	25.6	0.3
FUR	CORONA	0.4	0.3	0.2	-27.2	-0.1
CHERY	INDCHEMIE HEALTH SPECIALITIES PVT. LT	0.1	0.1	0.0	9.6	0.0
FERRO ATE M	LUPIN LTD	0.0	0.0	0.0	-100.0	0.0
FERINCA	SUN PHARMA LABORATORIES LTD.	0.0	0.0	0.0	-100.0	0.0
UNKNOWN	UNKNOWN	10.0	12.6	8.21	26.0	2.6

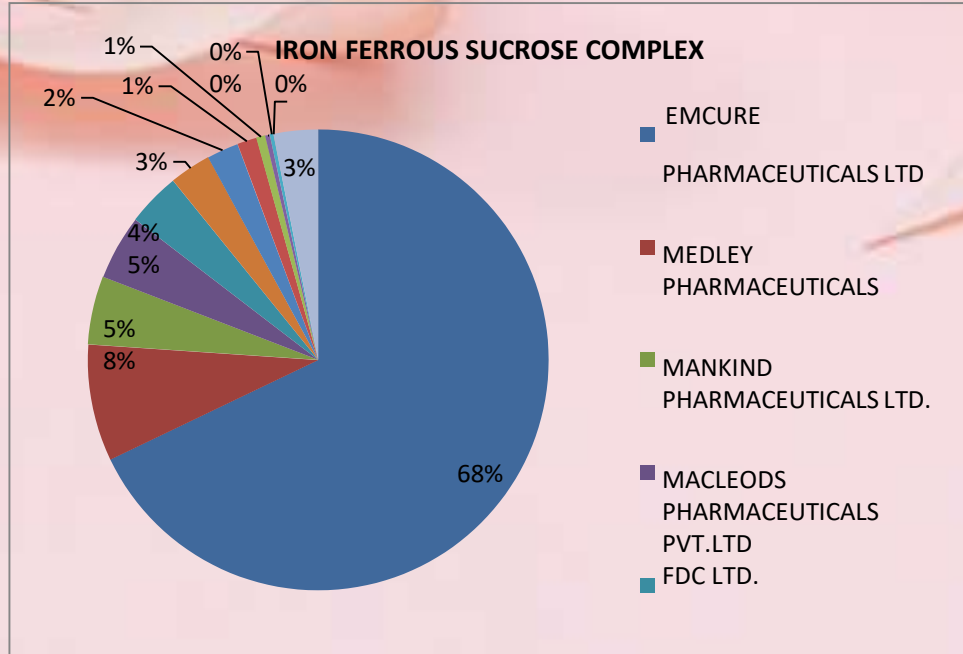
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ANALYSIS:

Raptakos brett and co. ltd. Showed highest market share percentage in combination of iron cynocobalamin and folic acid , having a brand name of Hepatoglobine approx 28% market share , Growth Rate of 4.6%, with the value added to the revenue of company in the revenue of company of 1.9 Cr in a year.

2. Iron Ferrous sucrose complex

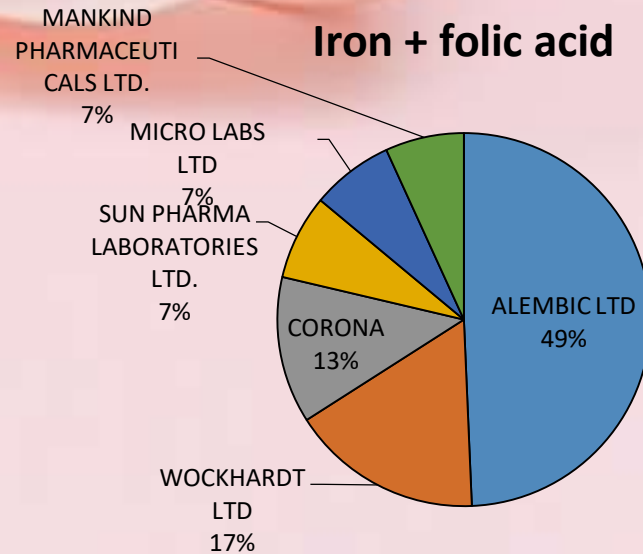


IRON FERROUS SUCROSE COMPLEX /Brands	Company	MAT July'18 Val in Crs.	MAT July'19 Val in Crs.	MS (%)	GR (%)	Value Addition in a year
		121.5	130.3	100.0	7.3	8.8
OROFER-S	EMCURE PHARMACEUTICALS LTD	81.2	88.4	67.9	8.9	7.3
R.B TONE	MEDLEY PHARMACEUTICALS	6.5	10.7	8.2	65.1	4.2
FERIKIND S	MANKIND PHARMACEUTICALS LTD.	5.8	6.3	4.8	8.1	0.5
RUBIRED S	MACLEODS PHARMACEUTICALS PVT.LTD	5.9	5.9	4.5	0.3	0.0
VITCOFOL S	FDC LTD.	5.0	4.9	3.7	-3.2	-0.2
IROZORB S	MACLEODS PHARMACEUTICALS PVT.LTD	3.6	3.8	2.9	5.7	0.2
MICROFER	MICRO LABS LTD	5.3	2.9	2.2	-45.8	-2.4
ANOFER S	SUN PHARMA LABORATORIES LTD.	1.7	1.8	1.4	2.3	0.0
HB 29	CORONA	0.9	0.8	0.6	-2.5	0.0
I-FAG	AKUMENTIS HEALTHCARE LTD	0.4	0.4	0.3	3.6	0.0
ROSEUS	AKUMENTIS HEALTHCARE LTD	1.1	0.3	0.3	-68.4	-0.7
WOFER S	WOCKHARDT LTD	0.0	0.0	0.0	-100.0	0.0
UNNOWN		4.2	4.1	3.1	-2%	-0.1

ANALYSIS:

Emcure was leading company with a largest percentage of market share , 68 % having a brand name OROFER-S , Growth Rate 8.9% and value added to the revenue of company, 7.3 Cr in a year.

3. Iron+ folic acid



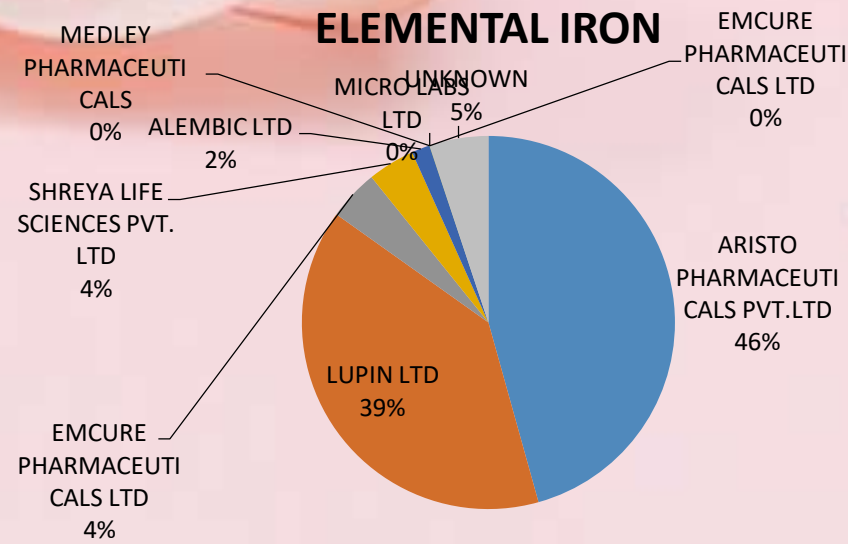
IRON + FOLIC ACID /Brands	Company	MAT July'18 Val in Crs.	MAT July'19 Val in Crs.	MS (%)	GR (%)	Value Addition in a year
		98.9	93.0	100.0	-5.9	-5.9
RICHAR	ALEMBIC LTD	28.7	30.3	32.6	5.9	1.7
PP 26	WOCKHARDT LTD	6.8	10.2	11.0	51.2	3.5
FUR XT	CORONA	7.0	7.8	8.4	11.9	0.8
SPEEDRAL	SUN PHARMA LABORATORIES LTD.	3.6	4.5	4.9	25.7	0.9
FEROX XT	MICRO LABS LTD	4.1	4.4	4.7	6.7	0.3
FERIKIND	MANKIND PHARMACEUTICALS LTD.	4.1	4.2	4.5	2.7	0.1
OROFER	EMCURE PHARMACEUTICALS LTD	3.8	3.9	4.2	4.7	0.2
IMAX XT	ARISTO PHARMACEUTICALS PVT.LTD	2.9	3.3	3.5	13.3	0.4
FERIUM XT	EMCURE PHARMACEUTICALS LTD	8.2	2.9	3.1	-64.3	-5.2
FUR	CORONA	1.2	2.9	3.1	133.2	1.6
BIOFER XT	MICRO LABS LTD	1.4	1.5	1.6	6.0	0.1
ZEBITA XT	INDCHEMIE HEALTH SPECIALITIES PVT. LT	0.7	0.8	0.8	15.9	0.1
ZIFOL XT	MICRO LABS LTD	0.7	0.7	0.8	-5.7	0.0
RICHAR XT	ALEMBIC LTD	0.7	0.6	0.7	-4.3	0.0
IRENTIA	AKUMENTIS HEALTHCARE LTD	0.4	0.1	0.1	-74.0	-0.3
FERIUM XTDHA	EMCURE PHARMACEUTICALS LTD	0.1	0.1	0.1	-35.6	0.0
VITCOFER	FDC LTD.	0.1	0.1	0.1	-17.0	0.0
VITCOFER SYP	FDC LTD.	0.0	0.1	0.1	503.8	0.0
ENCIFER O	EMCURE PHARMACEUTICALS LTD	0.1	0.0	0.0	-98.9	-0.1
IMAX	ARISTO PHARMACEUTICALS PVT.LTD	0.0	0.0	0.0	-84.9	0.0
OROFER-XT	EMCURE PHARMACEUTICALS LTD	11.4	0.0	0.0	-100.0	-11.4
Unknown	Unknown	13.1	14.6	15.7	11%	1.5

ANALYSIS:

Alembic ltd. Showed highest percentage of market share of combination of iron+ folic acid , approx 33% with the brand name of RICHAR , Growth Rate 5.9% and value added to the revenue of company, 1.7 Cr in a year.

4. Elemental Iron :

ELEMENTAL IRON



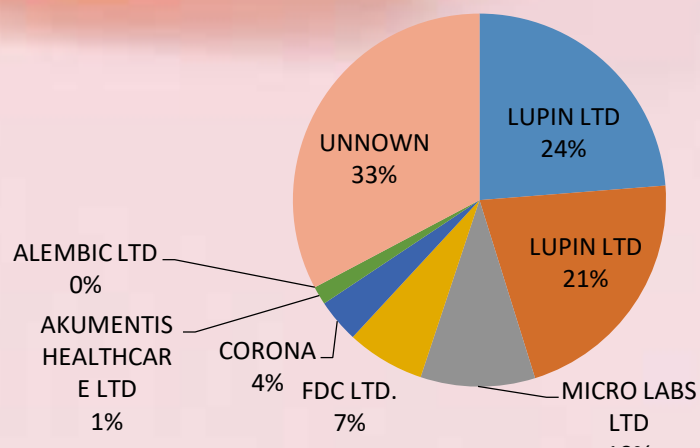
ELEMENTAL IRON /Brands	Company	MAT July'18 Val in Crs.	MAT July'19 Val inCrs.	MS (%)	GR (%)	Value Additio n in a year
		70.0	70.0	100.0	0.0	0.0
IMAX S	ARISTO PHARMACEUTICALS PVT.LTD	36.7	32.0	45.7	-13.0	-4.8
LUPIHEME	LUPIN LTD	21.3	27.4	39.2	28.8	6.1
FERRI	EMCURE PHARMACEUTICALS LTD	3.5	3.1	4.4	-12.5	-0.4
IMFERON S	SHREYA LIFE SCIENCES PVT. LTD	2.0	2.8	4.1	40.7	0.8
RICHAR XT	ALEMBIC LTD	1.1	1.1	1.6	0.6	0.0
ENCIFER	EMCURE PHARMACEUTICALS LTD	0.6	0.0	0.0	-96.7	-0.6
HBRON	MEDLEY PHARMACEUTICALS	0.0	0.0	0.0	0.0	0.0
BIOFER	MICRO LABS LTD	0.0	0.0	0.0	0.0	0.0
	UNNOWN	4.7	3.6	5.1	-23%	-1.1

ANALYSIS:

Aristo Showed highest percentage of market share approx 46%, with the brand name of IMAX-S , and Growth rate of -13%

5.Iron Ferric

IRON FERRIC



IRON FERRIC /Brands	Company	MAT July'18 Val in Crs.	MAT July'19 Val inCrs.	MS (%)	GR (%)	Value Addition in a year
		30.2	34.5	100.0	14.2	4.3
JILAZO	LUPIN LTD	8.8	8.2	23.76	-7.0	-0.6
ISOFER	LUPIN LTD	7.3	7.4	21.42	1.7	0.1
FERISOME	MICRO LABS LTD	3.4	3.4	9.93	2.2	0.1
VITCOFOL HB	FDC LTD.	3.1	2.3	6.77	-25.2	-0.8
HB 29 X	CORONA	0.0	1.3	3.77	0.0	1.3
HAEMADAY	AKUMENTIS HEALTHCARE LTD	0.3	0.5	1.59	75.9	0.2
KINPHOS	ALEMBIC LTD	0.1	0.0	0.00	-99.4	-0.1
	UNNOWN	7.2	11.3	32.3	57	4.1

ANALYSIS:

Lupin showed highest % of market share approx 24%, with the brand name of LILAZO and Growth rate of -7%

Pipeline Review:

By competitive profiling

➤ **Iron polymaltose complex-** can be a focused product which have growth rate of (27.4%)

Ferric carboxymaltose a novel iron complex that consists of a ferric hydroxide core stabilized by a carbohydrate shell allows for controlled delivery of iron to target tissues Administered intravenously.

It consist minimal risk of release of large amounts of ionic iron in the serum. It is an effective treatment for IDA in pregnancy.

➤ **Ferrous combination-** is most common molecule in other competitors with good MAT19 value (18.7 CR) and highest GR (409.8%)

➤ **Sucrosomial iron-** Sucrosomia Iron (SI) is an innovative oral iron formulation in which ferric pyrophosphate is protected by a phospholipid bilayer plus a sucrose matrix (sucrosome)

It absorbed through para-cellular and trans-cellular routes (M cells). This confers SI's unique structural, physicochemical and pharmacokinetic characteristics, together with its high iron bioavailability and excellent gastrointestinal tolerance.

Conclusion:

- According to WHO that approx 2 billion approx (50%) pregnant women's are anemic. In developing countries like India, 50 to 53 % pregnant women's are anemic
- . IDA adversely affects the maternal and fetal well-being, high risk for preterm delivery, fetal growth retardation, low birth weight, and inferior neonatal health, and is linked to increased fetal death.
- Manage Iron deficiency anemia oral and parental iron therapy is commonly used, both the therapy has adverse effects and iron overload in tissues and iron deficiency in blood.
- Lactoferrin represents an attractive and promising alternative to ferrous sulfate oral administration. Adverse effect of lactoferrin is lesser than ferrous therapy.
- oral Lf significantly improved the number of red blood cells, hemoglobin, total serum iron, and serum ferritin concentrations compared to those detected in pregnant women sub-optimally treated with ferrous preparations.
- Iron supplementation is required during the whole duration of pregnancy, so the effective treatment with lesser or no side effects and cost effective, should be focused.

CONT:

- Focus on other micronutrient combination needed during pregnancy.
- Requirement of iron during pregnancy influences by trimester and also by other internal factors (disease state, age, previous number of pregnancies), external factor (socioeconomic factors), so the supplementation should be given accordingly
- Role of ferroportin and hepcidin should also consider.
- Market of Haematinics is wide with various iron molecules; total Mat 19 value of market was approx 21.562 billion. According to the data and report combination of Iron cyanocobalamin and folic acid is the leading molecule
- IDA in pregnancy is readily manageable yet an unmet health demand. The management strategy is dependent upon the period of gestation and severity of anemia. Widespread implementation of preventive and therapeutic strategies is still lacking in our country. Organization of awareness camps, patient group meetings and the use of social media can spread awareness of this public health issues.



THANKS!!