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FORMULATION, OPTIMIZATION, AND IN VITRO RELEASE OF BOSWELLIA SERRATA (65% API) CAPSULE: A NOVEL HERBAL MEDICINE FOR OSTEOARTHRITIS

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ABSTRACT

Boswellia serrata (BS) is a well-known herbal medicine for osteoarthritis. It is one of the most potent herbal medicines. It has been used as a traditional medicine for the treatment of arthritic diseases. The present study was aimed to formulate, evaluate, and enhance the solubility profile of boswellia serrata (65% api) and make a capsule dosage form. It is prepared by solid dispersion and solvent evaporation using, tween 80 and tpgs as emulsifiers. The solubility profile of the capsule was evaluated by hardness test, friability study, disintegration time, and in vitro dissolution study. It was found that the optimized formulations, f11 capsule, api capsule, and control api capsule showed acceptable solubility and high permeability. So, it is concluded that using the TPGS as potent surfactant the capsule showing acceptable solubility, in-vitro drug release was significantly improved. The drug release was significantly improved, and the disintegration time was found to be 5 times greater. The results showed that the formulation f11, api capsule, and control api capsule showed acceptable solubility. So it concluded that the optimized formulation having enhance solibility and highly permeability.

KEYWORDS: Boswellia serrata (BS), surfactant, emulsifier, tpgs, tween 80, solvent evaporation, osteoarthritis, in vitro dissolution, solubility, permeability, cumulative release, frankincense.

1. INTRODUCTION

One of the most potent herbal medicines is Boswellia serrata (BS) extract, which is popularly known as the sallaki, indigenous olibanum of frankincense, and luban. Tropical areas of Africa, Asia, and the Arabian Peninsula are where BS is frequently cultivated. It is used in the Ayurvedic, Siddha, and Unani systems of traditional medicine. The dry exudate from the Boswellia trees bark is a resin of the oleo gum. Synonyms: Indian frankincense, Boswellia glabra Roxb.[1] A 15-foot-tall, resinous, evergreen tree called frankincense has papery, peeled bark. It has Five-petaled, creamy-white flowers appear in the spring followed by 3 to 5 angled, red-brown seed capsules.[2] The leaves are like neem plant and have small white flowers.[3] Wild trees are harvested for their oleo-gum resin by creating slits in their bark on the trunks and thick branches. When exposed to the outside air, the gum resin oozes from the incision spot and forms into an uneven mass. The oleo-gum-resin is collected all year and used freshor dried.[4] It is a gum extract from the Boswellia tree that is powdered and contains a variety of Boswellic acids. For the treatment of inflammatory illnesses, ayurvedic medicine has employed the gum resin from the Boswellia serrata tree.[5] It is an oleo-gum resin of Boswellia serrata, belonging to the Burseraceae family and consists of 17 genera and 600 species such as Boswellia carteri, Boswellia sacra, and Boswellia papyrifera.[6] The word olibanum, which refers to the Indian frankincense tree, is derived from the Arabic word al-luban, which means milk. Furthermore, it has been suggested that the name olibanum derives from the Arabic phrase for "Oil of Lebanon," as that is where the resin was exchanged with Europeans and where it was sold.[7] The English word is derived from old French “francencens” (i.e. high-quality incense) and is used in incense and perfumes.[8]

1.1. Chemical constituents

The identification of thirty-five constituents in yellow volatile oil of Boswellia serrata done by hydrodistalliation of bark of Boswellia serrata. The content and composition may vary by species depending on age, resin quality, and geographical condition. Oleo gum resin of BS has numerous active chemical constituents and pharmacologically active elements such as terpenoids and oil.[9] The oleo gum contains resins (30–60%), essential oil (5–10%), and water- soluble polysaccharides (~65% arabinose, galactose, and xylose) (BS monograph 2008). The essential oil of Salai guggul mainly contains monoterpenoids (α-pinene, cis-verbenol, trans- pinocarveol, borneol, myrcene, phellandrene, cadinene, verbenone, limonene, and a small amount of diterpenes). α-pinene (73.3%) is the major chemical constituent of monoterpenoid.[10] The Boswellia serrata bark oil prevalently contains monoterpenoids which

includes **α- Pinene (73.28 %), β- Pinene (2.05 %), cis-Verbenol (1.97 %), transpinocarveol (1.80 %),borneol (1.78 %), myrcene (1.71 %), verbenone (1.71 %), limonene (1.42 %), thuja- 2,4(10)-diene (1.18 %) and p-cymene (1.0%),** while α -copaene (0.13 %) was the only sesquiterpene identified in the oil.[11] The oleo-gum-resin have major of higher terpenoids (25-30%). The resinous part of Boswellia serrata contains monoterpenes (α-thujene); diterpenes (macrocyclic diterpenoids such as incensole, incensole oxide, iso- incensole oxide, a diterpene alcohol [serratol]); triterpenes (such as α- and β-amyrins); pentacyclic triterpenic acids (Boswellic acids); tetracyclic triterpenic acids (tirucall-8,24-dien- 21-oic acids). The confirmed the structure of methyl ester of acetyl- β-Boswellic acid found in 1995.[12] Several more triterpenoid compounds have been extracted from the gum resin in addition to Boswellic acid. This compound includes α- amyrins, 3 hydroxyl urs-9, 11-keto- α- Boswellic acid, 11- dien-24-oic acid. Tetracyclic triterpenoid acid compound also found in Boswellia serrata essential oil.[13]

1.2. Active ingredients of boswellia

A sample of Kundru analyzed **by Imperial Institute London** showed the following composition: **Moisture-10-11%, volatile oil 8-9%, resins 55-57%, Gum 20-23%, Insoluble matter 4-5%. The constituents are fixed oil, Terpenoids (three triterpene acids α, β and γ Boswellic acids** using barium hydroxide as precipitant) and Gum.[14]

Among the medicinal properties of Boswellia serrata are well-known anti-inflammatory ones, particularly for osteoarthritic diseases.

The number of carbon atoms in the end molecule determines how different terpenes are in response to the quantity of complete isoprene molecules used in synthesis.:

- C10 monoterpenes > (essential oils);
- Sesquiterpenes C15 > (essential oils);
- Diterpenes C20 > (gibberellins, resins);
- Triterpenes C30 > (b-Boswellic acid, glycyrrhizin, escin, madecassic acid);
- Tetraterpenes C40 > (carotenoids).

Boswellic acids are considered the main active constituents of Boswellia, with the predominant chemical form being beta form. The substance that has the greatest level of activity of the terpenic mixture is 11-keto-beta-boswellic acid, also known as AKBA. The currently available extractsare considered as Boswellic acids, ranging from 35 to 65%, and the

most active ones are thosewith the highest titration in AKBA.[15]

1.3. Mechanism of action

Table 1: Mechanism of action BS.

Sl no	Activity	MOA	Formulations
1	Anti-inflammatory	↓ 5-LO, ↓ 5-LOX ↓ COX-2 ↓Pro-inflammatory cytokines ↓ TNF-α, ↓ IL-β	Tablet/herbal gel/
2	Antimicrobial	↓ Antimicrobial peptide LL-37	Gel/cream/silver nanoparticle
3	Anticancer	↓ NF-κB AKBA ↓ VEGFR2 methylation-silencing tumor suppressor genes are activated and demethylated.	Solid lipid nanoparticle
4	Improvingmemory	↑ GSH content	Tablet
5	Improving memory	Regulating the Nrf2/ HO-1 pathway	Silver nanoparticles

- inhibition of leukotriene synthesis by specific action on 5-lipoxygenase;
- inhibition of HLE (human leukocyte elastase);
- inhibition of TNF-a and interleukin (PMN leukocyte chemotactic restriction);
- analgesic activity (inhibition of LTC4, LTB4, TNF, IL-1).[16]

BAs are characterized by their ability to act on multiple targets which are compiled in Table.

Table 2: Effect of boswellic acids on various organs.

Organ and functional system	Effects
Cardiovascular system	Cardiotonic
Gastrointestinal tract	Carminative, Regulating color of stoolAnthelmintic Improving digestion
Nervous system	Mental tonic Analgesic Eye tonic
Fever	Antipyretic
Skin	Increases perspiration Wound healing
Urogenital system	Diuretic Improving menstruation
Whole organism	Anti-inflammatory, Antiseptic, Reducing fat

1.4. Dosage

Boswellia is often consumed orally in the form of a pill, tablet, or bark decoction. The dosage is suggested based on past usage or current clinical investigations. Right now, it's unclear what dosage balances safety and effectiveness. It is more challenging to standardize Boswellia products because the production process varies from one item to another. It is important to note that most of the trials used various products made by various

manufacturers, so clinical effects may not be comparable.[17]

2. MATERIALS AND METHODS

2.1. Experimentation work

2.2. Aim & objective of the research work

- The aim of present study to formulate, evaluate and enhancement the solubility profile ofBoswellia serrata(65% api) and make a capsule dosage form.
- Among the all-osteoarthritis drug the drug boswellia serata is a potential anti-inflammatory drug.
- Boswellia serata having the main constituent is boswellic acids.
- Boswellic acids that inhibits 5-lipoxygenase with anti-inflammatory and anti-arthritic effects.
- Boswellia serrata is a bcs class -IV drug, having low solubility and low permeability.
- objective: enhancement of drug solubility with a proper dosage form for oral drug delivery.

2.3. Drug profile of boswellia serata

2.3.1.The main chemical constituent of boswellia serata is boswellia acids

Class: non-steroidal anti-inflammatory agent.

- The boswellic acids are organic acids, consisting of a pentacyclic triterpene, a carboxyl group and at least one other functional group.
- Alpha-boswellic acid and beta-boswellic acid, C30H48O3 both have an additional hydroxyl group; they differ only in their triterpene structure.
- Acetyl-alpha-boswellic acid and acetyl-beta-boswellic acid, C32H50O4, replace the hydroxyl group with an acetyl group.
- Other boswellic acids include the keto-boswellic acids and their acetyl counterparts.

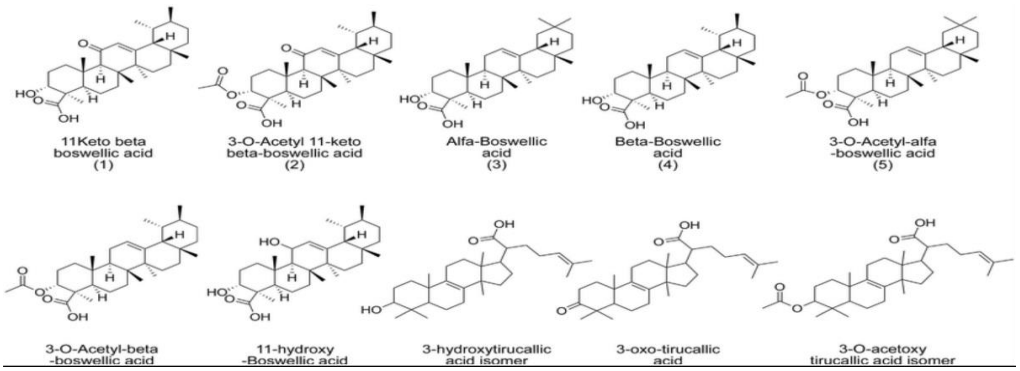

Figure 1: Structures of boswelic acids.

2.4. Structures of boswellic acids

- **Solubility:** Extracts of gum resin from Boswellia serrata are generally resinous in nature, and Boswellic acids (lipophilic compounds) are insoluble in water. soluble in methanol, acetonitrile, hexene
- **BCS CLASS-** IV
- **Half–life-** 6-8 HR
- **Route of administration- ORAL, TOPICAL**
- **EXPERIMENTAL DRUG NAME- BOSWELLIA SERATA 65% (**it is not a pure drug, contains only 65% drug & other is maltodextrin 35%**)**

2.5. Experimentation

Table 3: Preformulation studies.

Sl.No	Parameter	Results
1	Bulk density	0.53 mg/ml
2	Tap density	0.67 mg/ml
3	Carr's index	20.89 %
4	Housner's ratio	1.264
5	Angle of repose	27˚

Table 4: Solubility profile of pure boswellia serata.

S.No.	Solvent	Solubility
1	Water	Slightly soluble
2	Methanol	Soluble
3	Hexane	Soluble
4	Dichloromethane	Soluble
5	Acetonitrile	soluble

Table 5: Solubility analysis of boswellia serata 65%.

Sl.No	Solvent	Result	Process
1	Methanol	Partially soluble	Sonication 10 min +30 c
2	Methanol 70+ Water 30	Partially soluble	Sonication 10 min +30 C+ Cyclomixing 5 min
3	Dmso	Fully soluble	Sonication 10 min +30 c
4	Dmso 0.4ml+water9.6	Milky colour	Sonication 10 min +30 c
5	Dmso 2+water 8	Less milky + Soluble	Sonication 10 min +30 c
6	Dmso 0.1+water9.9	Milky colour + agglomeration Particle	Sonication 10 min +30 c
7	Dmso 0.1+hexane 9.9	Phase separation Occur	Sonication 10 min +30 c
8	Hexane	Partially soluble	Sonication 10 min +30c+ Cyclomixing 5 min
9	Dmso	Milky color + Phase	Sonication 10 min +30 c

	0.1+acetonitrile 9.9	separation	
10	Acetonitrile	Partially soluble	Sonication 15 min +35c+ Cyclomixing 5 min
11	Acetonitrile 70%	Partially soluble	Sonication 15 min +35c
12	Acetonitrile 50%	Partially soluble	Sonication 120min +40c
13	Acetonitrile 60%	Partially soluble	Sonication 10min +35c
14	Dmso 0.1+ Acetonitrile 60%	Partially soluble, milky Colour	Sonication 10min +35c
15	Acetone	Partially soluble	Cyclomixing 5 min+ Sonication 10min 30c
16	Ethanol	Partially soluble	Cyclomixing 5 min+ Sonication 10min 30c
17	6.8 buffer	Partially soluble	Cyclomixing 5min+ Sonication 10min 30c
18	Water	Partially soluble	Sonication 10min 30c+cyclomixer 10 min

2.5.1. Determination of λmax (u.v method)

Drug (250 mg) was accurately weighed and dissolved in 50 ml of 6.8 BUFFER solutionin a FALCON TUBE. The solution is then ultrasonicated for 10 minutes at 40 degrees Celsius, followed by 15 minutes of centrifugation at 5000 rpm. The stock solution was pipetted into a 10 ml volumetric flask from the supernatant solution after which the volume was brought up to the required level using 6.8 BUFFER solution. The resulting solution was scanned between 200 – 400 nm using UV- Visible spectrophotometer (ShimadzuUV-1800, Japan).

The λmax was found to be 260 nm.

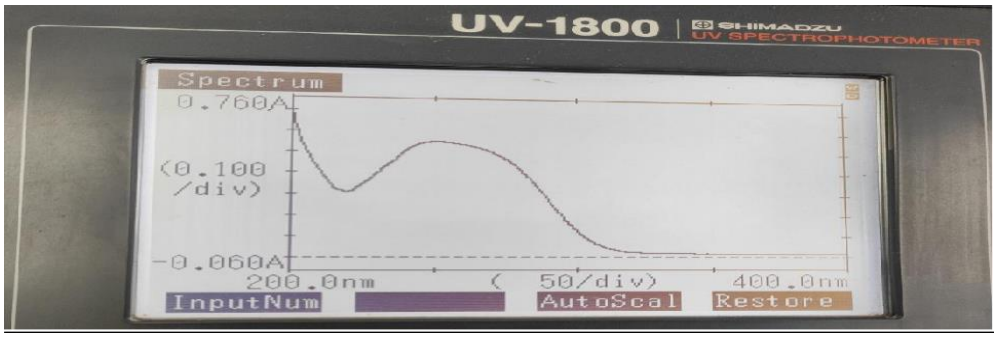

Figure 2: Determination of absorption maximum.

2.5.2. Calibration curve taking pure boswellia serata vs boswellia serata 65%

After finalize the λmax of the drug i.e., 260 nm, according to that the calibration curve will prepared.

We take two types of Boswellia Serrata product.

2.5.2.1. Preparation of standard curve of boswellia serata 65% in water solution

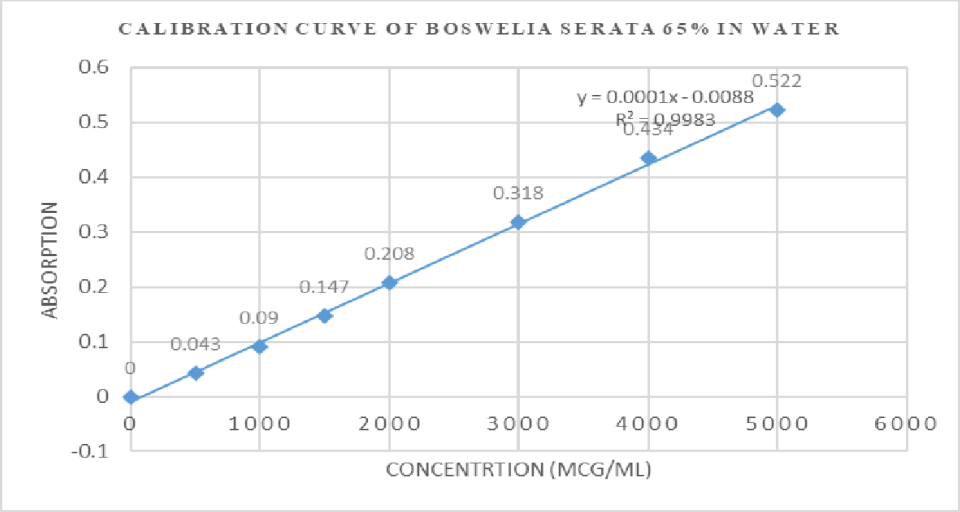

Figure 3: Standard curve of boswellia serata 65% in water solution.

2.5.2.2. Preparation of standard curve of boswellia serata 65% in 6.8 buffer

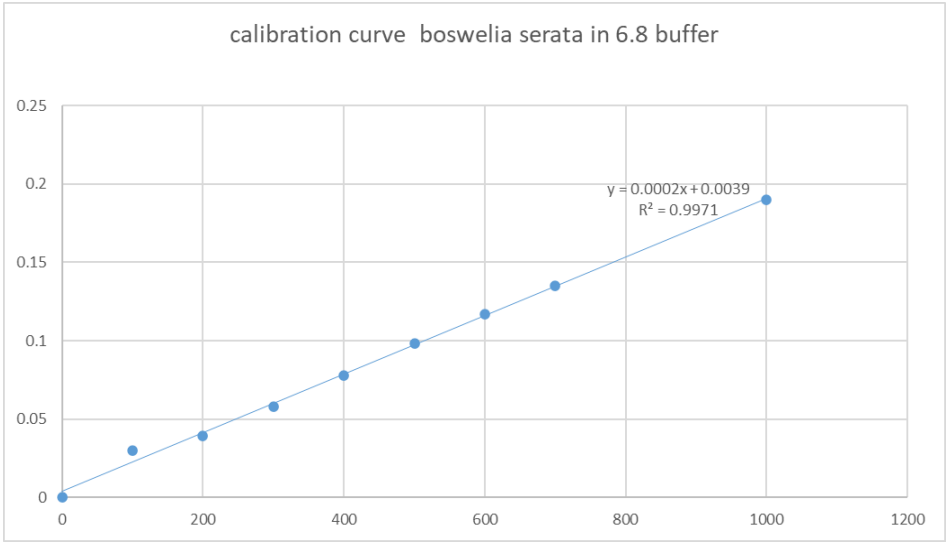

Figure 4: Standard curve of boswellia serata 65% in 6.8 buffer.

Result – analyzing above these two calibration curve of Boswellia serrta 65%, we decided to finalize the pure Boswellia serrta calibration curve.

2.5.2.3. Finalized calibration curve taking pure boswellia serrta extract

2.5.2.3.1.U.v plot of boswellic acid in ph 6.8 phosphate buffer solution

Calibration curve of boswellic acid through U.V.

The calibration curve of U.V. depicts that it obeys Beer's Lambert law where, slope = 0.0026 and R2 = 0.9947 at 260 nm. Formula - x=y+0.006/0.002It is the finalize calibration curve for further experiment.

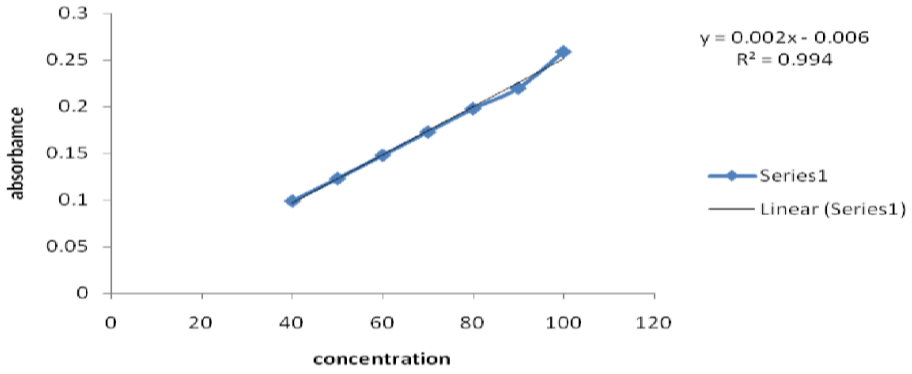

Figure 5: Finalized calibration curve of boswellic acid in ph 6.8 phosphate buffer solution.

Table 6: Ph of boswellia serrate.

Sr. No.	Solvent Media	Boswelia serata in mg/ml
1	water	3.8

A semi quantitative determination of solubility can be made by adding a solute in small incremental amounts to fixed volume of solvents whose pH are.

2.5.3. Infrared spectroscopy

2.5.3.1. Fourier-transform infrared spectroscopy

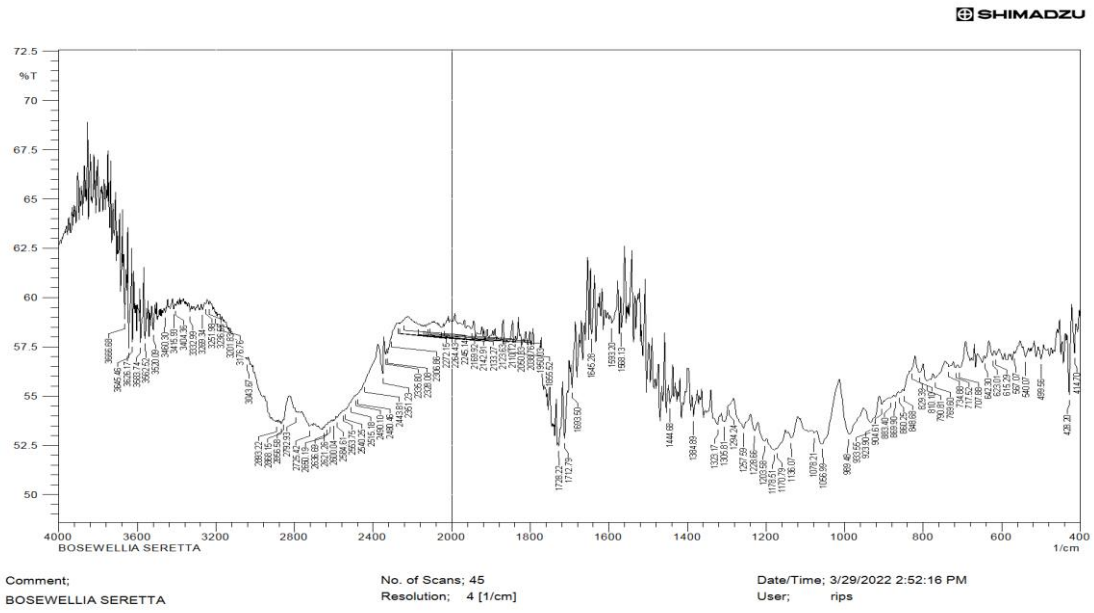

Figure 6: Ft-ir spectra of boswellic acid extract.

2.5.4. Differential scanning calorimetry (DSc) study

Figure 7: DSc study of B.serrata.

The extract's melting point was discovered to be 239.575°C which is in accordance with the standard monograph (238.122°C) of boswellic acid which confirms the presence of Boswellic acid in the extract of B.serrata.

2.6. Formulations table of boswellia serata 65% powder api

Table 7: Formulation table.

Ingredients	Amount(mg/tablet)											
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Boswellia serata	85	80	85	85	88	85	85	85	85	85	88	90
Tween 80	5	2	--	---	-	-	2	-	-	-	3	3
PVP	5	3	9	15	10	5	7	5	4	3	---	---
Propylene Glycol	5	-	-	--	-	-	--	---	--	---	---	---
Maltodextrin	5	15	--	---	---	---	--	----		---	---	----
SLS	---	---	3	---	---	--	2	2	--	--	----	---
PEG 4000	---	---	3	---	---	----	4	3	4	3	----	----
QUILAJA	---	---	---	---	2	2	--	---	---	---	----	-----
Angel Potato starch	----	---	----	----	--	8	---	---	---	---	---	----
DFE Pregelatinized potato starch	---	---	---	---	---	---	---	5	---	--	---	---
TPGS	----	---	---	----	----	----	---	---	5	7	7	7
HPMC	----	----	---	----	---	----	---	--	2	2	2	
Total amount in mg	100	100	100	100	100	100	100	100	100	100	100	100

Some formulation time photo

Figure 8: Boswellia serata formulation.

2.7. Solubility study of boswellia serata in 6.8 buffer

2.7.1. Procedure

- Taking 12 number of 500 ml beaker and put in a water bath maintaining the body temp(37°C)
- In the beaker add the selective media (6.8 buffer) 300 ml in each, And taking a blank solution for maintain the sink condition.
- Add the formulation of Boswellia serrata (375 mg) in the beaker and compare to the standard.
- Taking 1 hr time interval the sampling will be done.
- Before sampling, continuous stirring is done for 5 min for each.
- After taking the sample the UV spectrophotometer absorbance data will record.
- As per the calibration curve data the concentration is calculated.

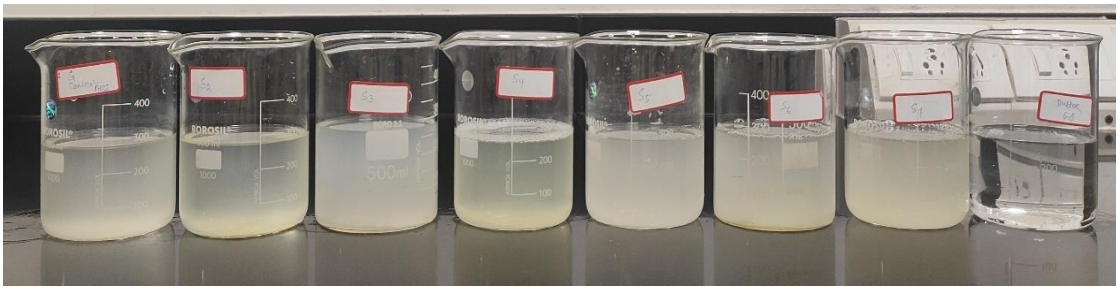

Figure 9: Solubility study of boswellia serata.

Sample1(S1)- Pure Boswellia Serrata Api, S2-f1 formulation, S3-f2 formulation, S4-f3 formulation, S5-f4 formulation, S6-f5 formulation, S7-f6 formulation, S8-f7 formulation, S9-f8 formulation, S10-f9 formulation, S11-f10 formulation. S12-f11 formulation, S13-f12 formulation.

Table 8: Concentration mcg/ml of Boswellia serrata 65% powder drug.

CONCENTRATION mcg/ml OF DRUG IN 6.8 BUFFER FORMULA- Y=0.002x-0.006													
TIME (hr)	**S1**	**S2**	**S3**	**S4**	**S5**	**S6**	**S7**	**S8**	**S9**	**S10**	**S11**	**S12**	**S13**
0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.5	91	100	102	156	118.5	140.5	134	393	171.5	254	613	288.5	300.5
1	68	125	128	165	103	144.5	116	230	187.5	248	372	382.5	329
2	59	116	117	144.5	101.5	111.5	100.5	184.5	137	269	330	411.5	381
3	63.5	124.5	129	155.5	116	129.5	131.5	173	107.5	276.5	326	413.5	383.5
4	60.5	120	123.5	145.5	90	114.5	121.5	200	130.5	301.5	374.5	433	402
5	65	122	132	166	112.5	155	136.8	161	114	286	338.5	448	419.5
6	91.5	149.5	162	201.5	150.5	146.5	163	181.5	133.5	316.5	340	435	403.5

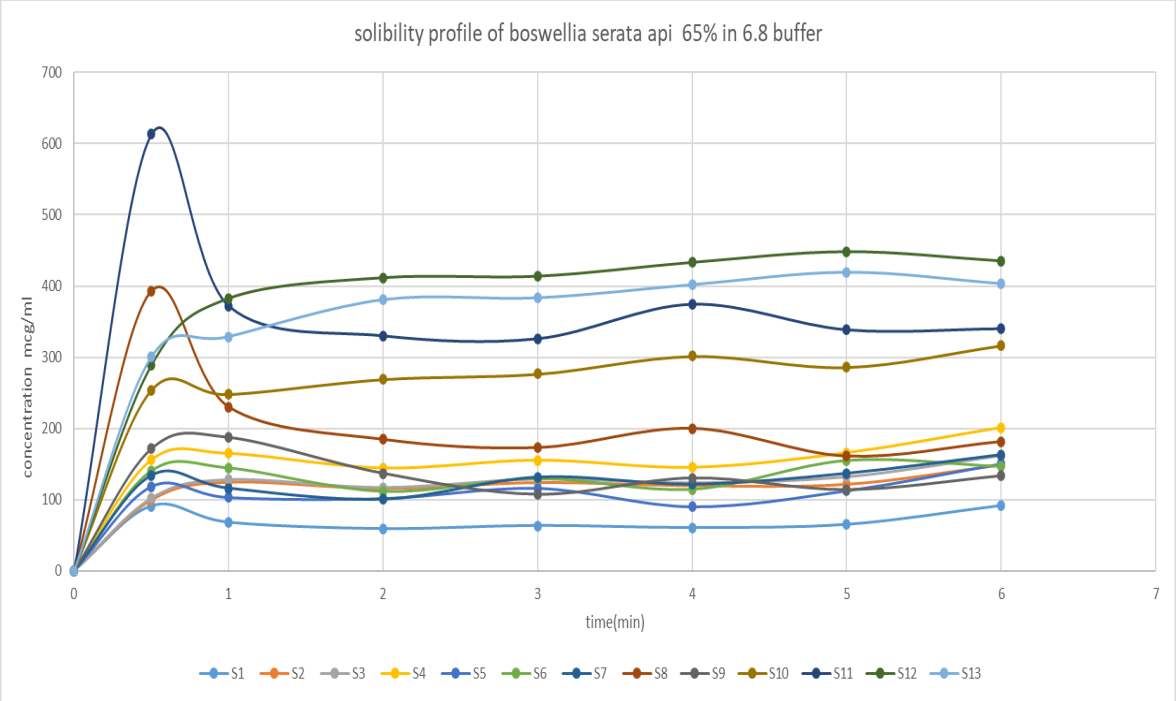

Figure 10: Solubility graph according to our formulation of boswellia serrata 65% powder drug.

- After see the solubility profile of above formulation drug we finalize the formulation 11 i.e., sample 12, for our further used.
- FORMULATION 11 CONTAIN DRUG+TPGS+TWEEN 80 +HPMC

Table 9: Brief discussion about formulation -11 powder drug.

BOSWELLIA SERATA 65 % FORMULATION			
	FORMULATION-11		
SL NO	**COMPOSITION**	**AMMOUNT**	**REQUIRED**
1	BOSWELIA SERATA	88	44
2	TWEEN 80	3	1.5
3	TPGS	7	3.5
4	HPMC	2	1
		100	50

2.8. Method of preparation of optimized formulation

2.8.1. Technique used

SOLID DISPERSION + SOLVENT EVAPORATION

SOLID DISPERSION- The term solid dispersion refers to the dispersion of one or more active ingredients in a hydrophilic inert carrier matrix at molecular level. It is prepared by the melt (fusion) method and solvent evaporation technique. However, the process is individualized depending on the interaction between drug and carrier.

SOLVENT EVAPORATION-In the solvent evaporation method, the drug is dissolved, dispersed, or emulsified into an organic polymer solution, which is then emulsified into an external aqueous or oil phase. The microspheres are formed after solvent diffusion/evaporation and polymer precipitation.

2.9. Preparation procedure of optimized formulation

DISTILED WATER 30 ML

↓

TPGS (BOIL 70°C FOR 5MIN)

↓

HOMOZINIZATION FOR 5 MIN

↓

TWEEN 80

↓

HOMOZINIZATION FOR 5 MIN

↓

API

↓

HOMOZINIZATION FOR 20 MIN

↓

HPMC

↓

HOMOZINIZATION FOR 10 MIN

↓

VACUMME DRYING AND LYOPHILIZING UPTO 12 HR AT 50 ° C

↓

MILLING AND SEAVING IN 120 MESH

↓

FINALIZED PRODUCT

2.10. Evaluation work of (f11) optimized formulation

Table 10: Drug release profile of (f 11) in 6.8 buffer.

Drug release profile of boswellia serata Optimized formulation (f11) in 6.8 buffer		
TIME	**DRUG RELESE MG/300 ML**	**% OF DRUGRELESE**
0	0	0
0.5	86.55	23.08
1	114.75	30.6
2	123.45	32.92
3	124.05	33.08

4	129.9	34.64
5	134.4	35.84
6	130.5	34.8

Table 11: Drug release profile of boswellia serata 65% api in 6.8 buffer.

Drug release profile of boswellia serata api in 6.8 buffer		
TIME	**DRUG RELESE MG/300 ML**	**% OF DRUG RELESE**
0	0	0
0.5	27.3	7.28
1	20.4	5.44
2	17.7	4.72
3	19.05	5.08
4	18.15	4.84
5	19.5	5.2
6	27.45	7.32

2.10.1. Physical evaluation f11 optimized boswellia serata 65% powdered drug

Table 12: Parameter table f11 formulated drug.

Sl.No	Parameter	Results
1	Bulk density	0.57 mg/ml
2	Tap density	0.64 mg/ml
3	Carr's index	10.93 %
4	Housner's ratio	1.12
5	Angle of repose	25˚

2.10.2. Result of solubility study - solubility is 35 % enhance as compare to standard api.

2.10.3. Hplc study of f11 boswellia serata

Table 13: Hplc data f11.

Column	C_{18} column
Mobile Phase	ACETONITRILE: WATER
Retention Time	11 MIN
Flow rate	1 ml/min.
ƛ max	250 nm
Injection volume	20 µL
Amount of AKBA%	0.202%

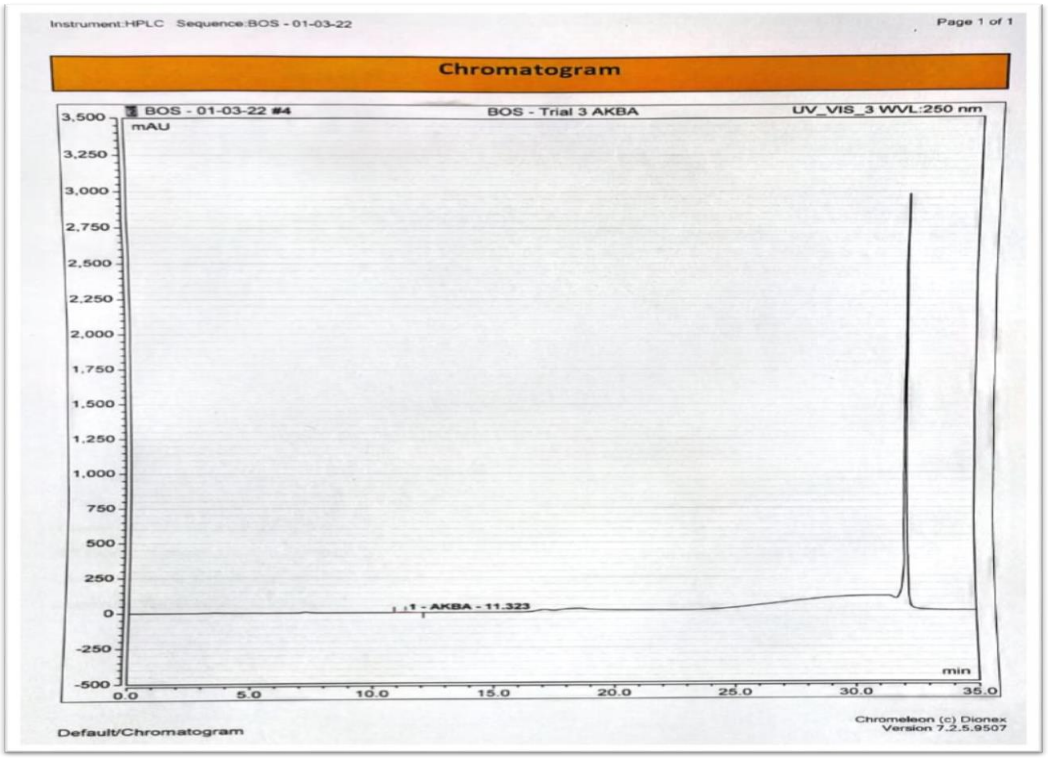

Figure 11: Hplc data of f11 drug.

2.10.4. Infrared spectroscopy

Fourier-Transform Infrared Spectroscopy

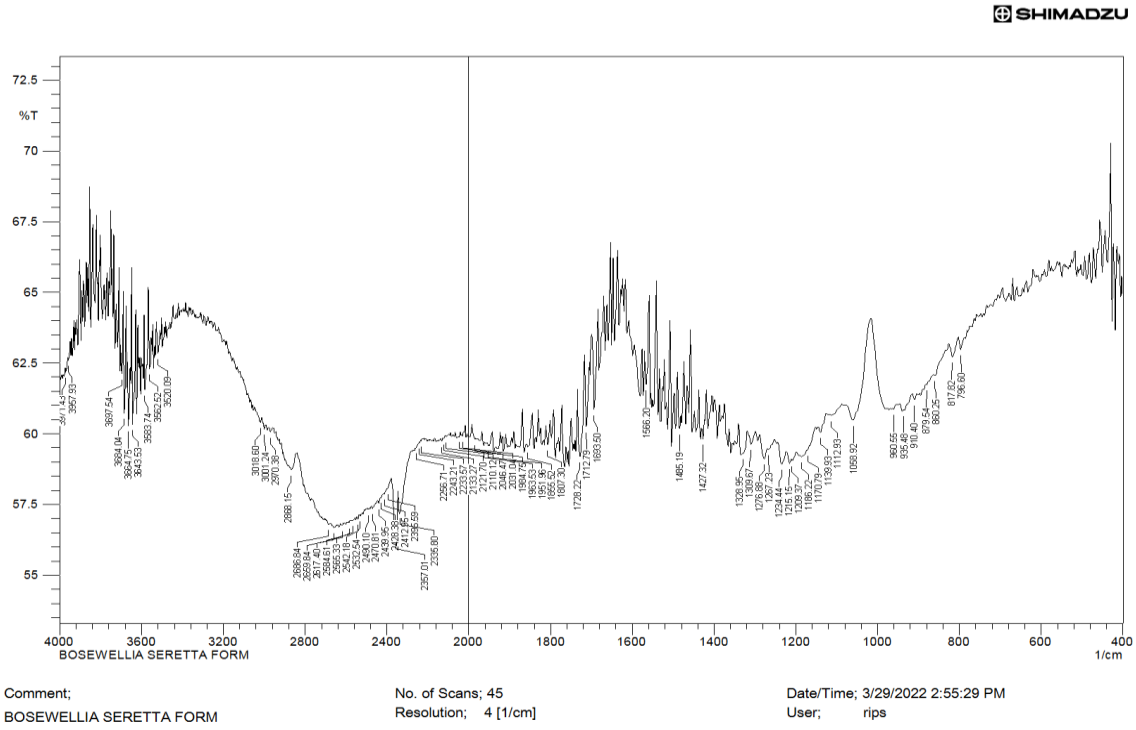

Figure 12: Fourier-transform infrared spectroscopy of f11.

Table 14: Interpretation FT-IR spectra of boswellic acid extract.

Wavenumber (Cm-1)	Characteristic Functional Group Feasible	Compound Type
2948.32	Ar C-H stretch	Aromatic
799.53	Ar C-H	Aromatic
1653.07	C=C stretch	Cycloalkenes
1700.32	C=0 stretch	Carboxyl
3461.48	O-H stretch	Hydroxyl

2.10.5. Differential scanning calorimetry (DSc) study

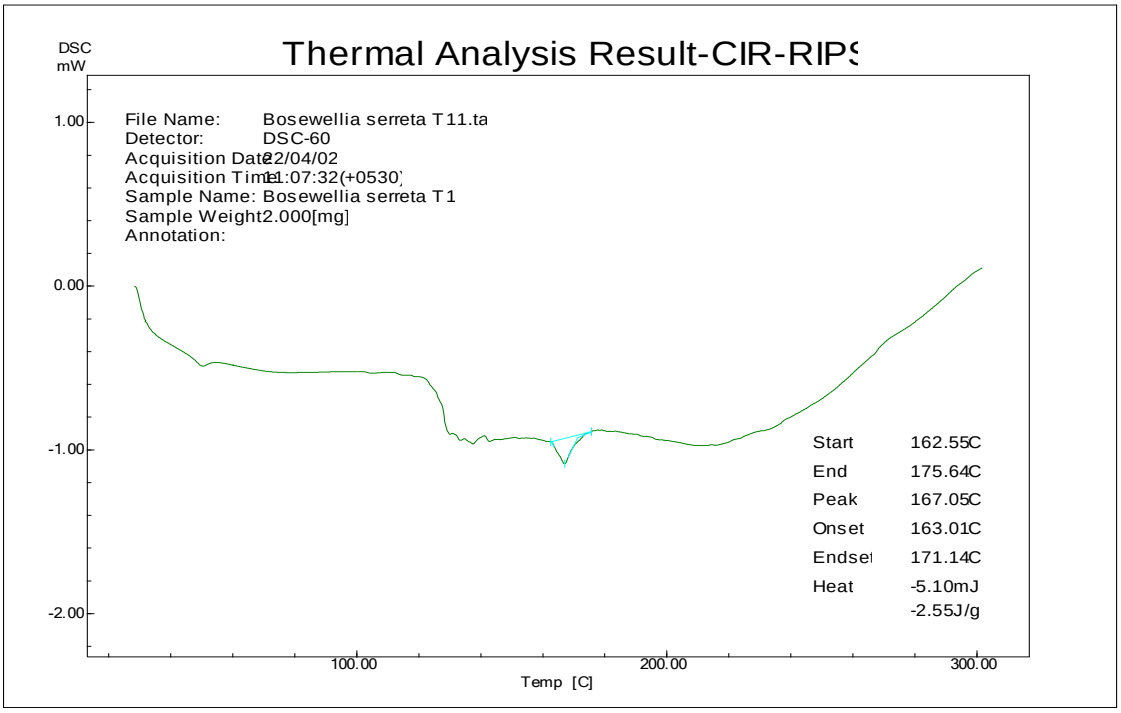

Figure 13: DSc data of f11 formulation.

The melting point of the extract was discovered to be 239.575°C which is in accordance with the standard monograph (238.122°C) of boswellic acid which confirms the presence of Boswellicacid in the extract of B. serrata.

2.11. Selection of suitable dosages form for formulated drug

- After successfully make the optimized formulation (f11), we decide to formulate a capsule dosage form for better release of the drug.

2.11.1. Preparation of capsule dosage form

- The optimized formulation f11, is accurately weighed (500mg for 1 capsule)
- For 50 capsule total weighed 25gm of drug powder.

- As per the sop, the drug filled in size 0 capsule by the Manual Capsule Filling Machine.
- According to the marketed capsule of different company, the dose was calculated.

Figure 14:-Size 0 capsule of Boswellia serata formulation.

2.11.2. Finalized capsule dosage form evaluation

Appearance

Capsules produced on a small or a large scale should be uniform in appearance. Visual or electronic inspection should be undertaken to detect any flaws in the integrity and appearance of the capsule.

2. Size and Shape

Hard capsules are made in a range of sizes, the standard industrial ones in use today for human medicines range from size from 000 (the largest) to 5 (the smallest) are commercially available.inspection must be done for size and shape.

3. Unique Identification Markings

Capsule surfaces may bear symbols or other unique identification markings for better identification.

Permeability and sealing

Hard gelatin capsules are tested whether it is breakage, opened(cap &body) or not.Result-it is perfectly sealed & no brokage is there.

2.11.2.1. Weight variation test

Table 15: Weight variation test for hard gelatin cap.

Sl. No.	Initial Weight	Average Weight (I.W/20)	% Of Weight (I.W/A.W×100)
2	605	603.3	100.2818
3	604		100.116
4	601		99.61876

5	602		99.78452
6	608		100.779
7	603		99.95027
8	607		100.6133
9	599		99.28725
10	608		100.779
11	600		99.45301
12	606		100.4475
13	608		100.779
14	585		96.96668
15	605		100.2818
16	601		99.61876
17	607		100.6133
18	606		100.4475
19	602		99.78452
20	599		99.28725

- Weigh 20 capsules individually & determine the average weight.
- The requirements are met if each of the individual weights is within the limits of 90% - 110% of the average weight.

- **Each of the individual weights is present within the limits of 90% -110% of the average weight.**
- **Capsules are passed Weight variation test.**

2.11.2.2. Disintegration test for capsules

- The disintegration test determines the whether capsules disintegrated with a prescribed time when placed in a liquid medium under the prescribed integral conditions.

Table 16: Disintegration limit.

Capsule	Medium	Time limit
Hard gelatin	Water/0.1M HCl/Artificial gastric juice	≤30 min

- In disintegration test, I take 6 capsules.

Table 17: Result of disintegration test

Si. No.	Disintegration Time (min)
1	10
2	12
3	9
4	10

5	11
6	9

- All 6 capsules are passed disintegration test.

2.11.3. In vitro dissolution

2.11.3.1. Dissolution study of api capsule and optimized formulation procedure

- First take the api and optimized formulation(f11) capsule.
- Take 300 ml of 6.8 buffer as dissolution media.
- Set the temperature of the media to 37° c
- Add the predetermine dose of boswellia serata optimized formulation capsule in to the dissolution media.
- According to the time interval (1 hr,2hr,3 hr……) 5 ml of sample of each container was taken simultaneously.
- After taking the sample, the sink condition was maintained by 6.8 buffer suddenly.
- The absorbance was measure by the u.v spectrophotometer of the taken sample.
- In a particular time period, how much absorbance is measure is listed in below table.

Table 18: Dissolution limit

DRUG PRODUCT	**API AND F11 CAPSULE**	
DISSOLUTION MEDIA	6.8 BUFFER 300 ML	
TIME INTERVAL	1 HR	
DISSOLUTION APPARETUS	Dissolution Tester(USP II)Electro lab (TDT06L)	
TEMP	37°C	
DOSE OF DRUG	375MG	
TIME OF STUDY	7 HR	
ABSORPTION PROFILE OF API & F11 CAPSULE IN 6.8 BUFFER		
TIME (HR)	API CAPSULE	F11 CAPSULE
0	0	0
1	0.063	0.496
2	0.096	0.598
3	0.128	0.685
4	0.132	0.795
5	0.139	0.821
6	0.154	0.869
7	0.176	0.882

CONCENTRATION PROFILE OF API & F11 CAPSULE IN 6.8 BUFFER (Y=0.002X-0.006)		
TIME (HR)	**API CAPSULE mcg/ml**	**F11 CAPSULE mcg/ml**
0	0	0

1	34.5	251
2	51	302
3	67	345.5
4	69	400.5
5	72.5	413.5
6	80	437.5
7	91	444

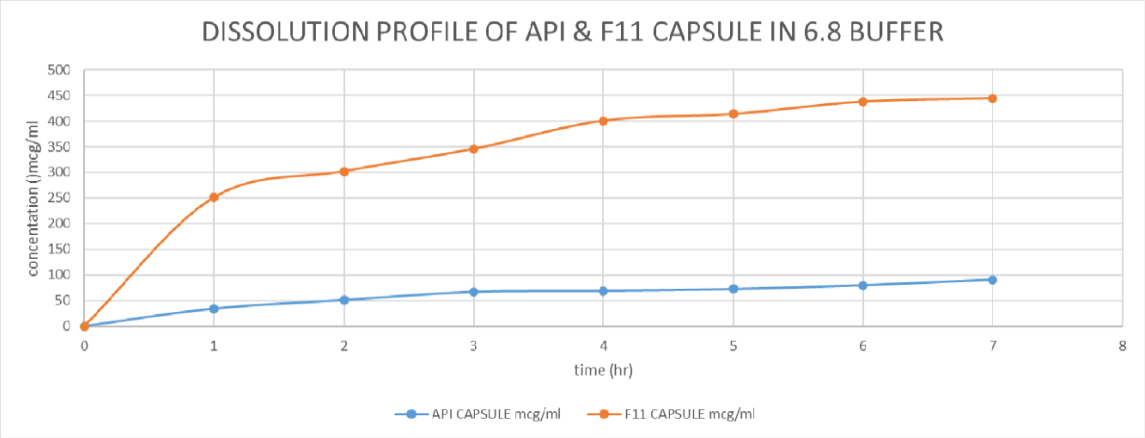

Figure 15: Final dissolution graph of api & f11 capsule.

Table 19: Drug release profile of api capsule and f11 capsule.

Drug release profile of boswellia serata api capsule in 6.8 buffer		
TIME	**DRUG RELESE MG/300 ML**	**% OF DRUG RELESE**
0	0	0
1	10.35	2.76
2	15.3	4.08
3	20.1	5.36
4	20.7	5.52
5	21.75	5.8
6	24	6.4
7	27.3	7.28

Drug release profile of boswellia serata Optimized formulation (f11) capsule in 6.8 buffer		
TIME	**DRUG RELESE MG/300 ML**	**% OF DRUG RELESE**
0	0	0
1	75.3	20.08
2	90.6	24.16
3	103.65	27.64
4	120.15	32.04
5	124.05	33.08
6	131.25	35
7	133.2	35.52

2.11.3.2. Comparison study

2.11.3.3. In vitro % drug release of boswellia serata (api,f11,api capsule, f11 capsule) in buffer 6.8

Table 20: In vitro drug release of api & f11 powder with api & f11 capsule.

PRODUCT	API,F11,API CAPSULE,F11 CAPSULE
DISSOLUTION MEDIUM	6.8 BUFFER,300ML
DRUG TAKEN IN CAPSULE	375 MG DRUG IN EACH PRODUCT

Amount of drug released mg/ ml = Concentration × Dissolution bath volume × dilution factor/1000.

% Drug Release = Drug Release/ Drug Taken * 100

Table 21: In vitro % drug release of api & f11 powder with api & f11 capsule.

% OF DRUG RELESE PROFILE OF API,F11,API CAPSULE& F11 CAPSULE IN 6.8 BUFFER				
TIME	B.S 65% API	B.S OPT. F11	API CAPSULE	F11 CAPSULE
0	0	0	0	0
1	5.44	30.6	2.76	20.08
2	4.72	32.92	4.08	24.16
3	5.08	33.08	5.36	27.64
4	4.84	34.64	5.52	32.04
5	5.2	35.84	5.8	33.08
6	7.32	34.8	6.4	35

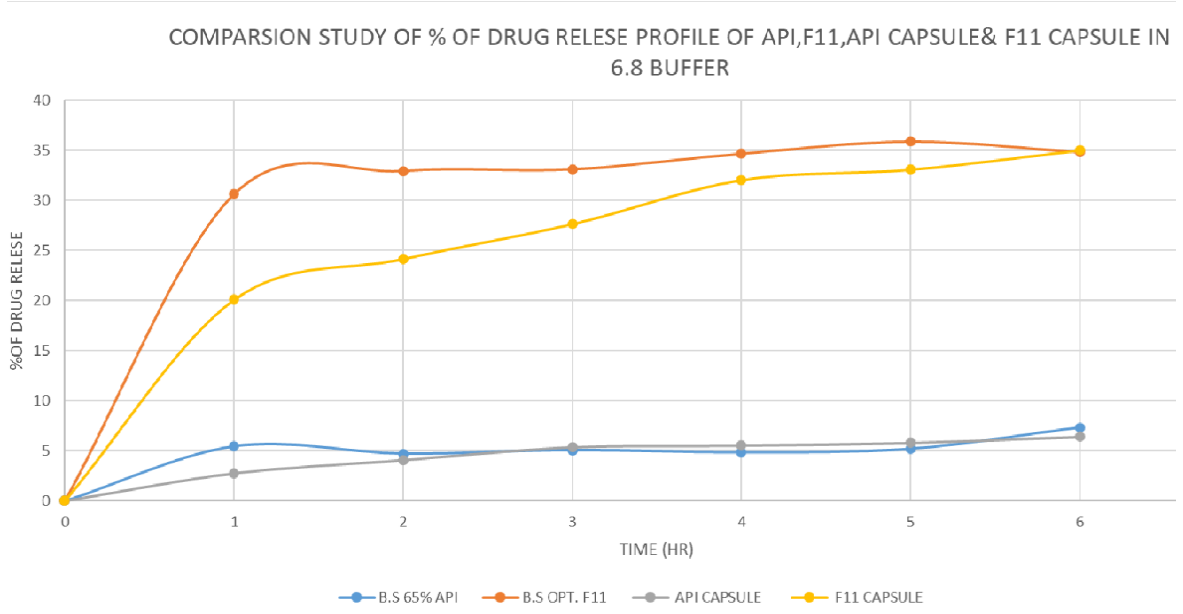

Figure 16: Comparison graph of api & f11 capsule with api & f11 powder.

2.11.3.4. In vitro cumulative drug release in buffer 6.8.

- First take the api and optimized formulation(f11) capsule.

- Take 300 ml of 6.8 buffer as dissolution media.
- Set the temperature of the media to 37° c
- Add the predetermine dose of boswellia serata optimized formulation capsule in to the dissolution media.
- According to the time interval (1 hr,2hr,3 hr.……) 5 ml of sample of each container was taken simultaneously.
- Sink condition not maintained.
- The absorbance was measure by the u.v spectrophotometer of the taken sample.
- In a particular time period, how much absorbance is measure is listed in below table.
- from absorbance the drug concentration in the media is calculated.

  Amount of drug released mg/ ml = Concentration × Dissolution bath volume × dilutionfactor/1000.

% Drug Release = Drug Release/ Drug Taken * 100

Table 22: Cumulative drug release profile f11 & api capsule in 6.8 buffer.

PRODUCT	API CAPSULE, F11 CAPSULE
DISSOLUTION MEDIUM	6.8 BUFFER,300ML
DRUG TAKEN IN CAPSULE	375 MG DRUG IN EACH PRODUCT

CUMULATIVE ABSORPTION PROFILE OF API & F11 CAPSULE IN 6.8 BUFFER		
TIME (HR)	**API CAPSULE**	**F11 CAPSULE**
0	0	0
1	0.113	0.326
2	0.196	0.498
3	0.198	0.685
4	0.203	0.725
5	0.219	0.829
6	0.324	0.859
7	0.366	0.862

CUMULATIVE DRUG RELESE OF API & F11 CAPSULE (MG)		
TIME	**API CAPSULE**	**F11 CAPSULE**
0	0	0
1	17.85	49.8
2	30.3	75.6
3	30.6	103.65
4	31.35	109.65
5	33.75	125.25
6	49.5	129.75
7	55.8	130.2

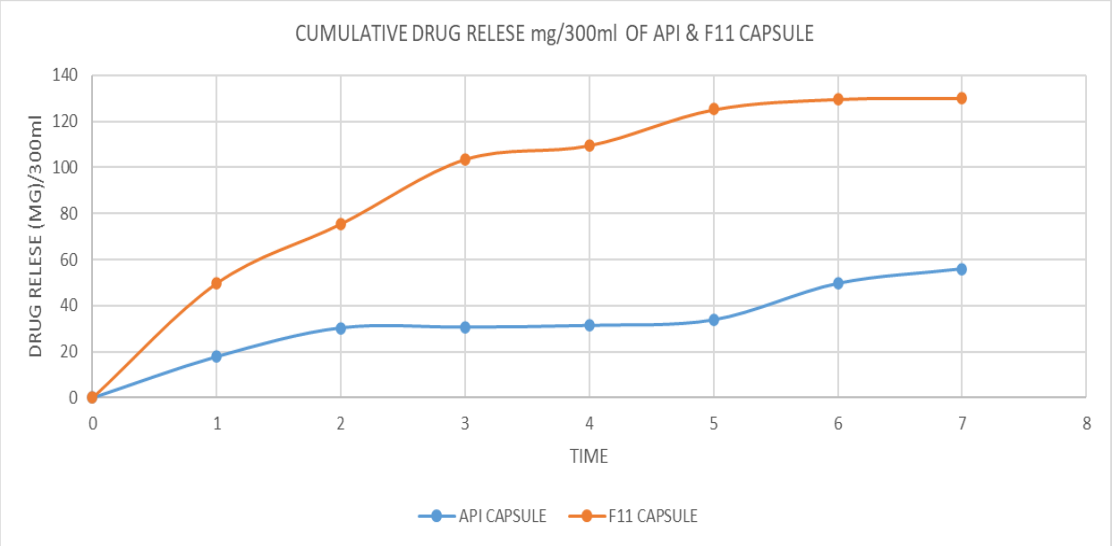

Figure 17: Cumulative drug release graph of api & f11 capsule.

3. RESULT AND DISCUSSION

- Capsule of Boswellia serata are prepared by solid dispersion and solvent evaporation method.
- Emulsifier like tween 80, TPGS, solubilizing agent like PVP, PEG and carrier like MALTODEXTRIN, POTATO STACH in different concentrations are used. 12 formulations and a control formulation were prepared.
- **Weight variation:** The capsules obtained were of uniform weight with acceptable official limits i.e., is within the limits of 90% -110% of the average weight.
- **Drug release studies:** Drug release studies were performed on the optimized formulation f11, api capsule & f11 capsule along with the control api reveals that the percentage drug release for the formulations f11 found to 34.8 %, f11 capsule found to 35% & control api capsule found to be 6.4% respectively once the final 6 hr. study. The control api release percentage found to be 7.32%. As compare to control, the optimized f11 capsule gives 5 times greater release.
- **Disintegration time:** Disintegration time for the formulations was found to range from 9-12 min. which facilitates their faster disintegration in the stomach which is subjected to further studies like In vitro dissolution which was carried out for optimization.

- **In Vitro Dissolution**

The in vitro dissolution study for the optimized formulations, f11 capsule as compare to control api is 5 times greater. For further increase of release % the experimental work is in process.

3.1. Summary

- Various emulsifier, surfactant, carrier such like Tween 80, Pvp, Peg, Maltodextrin were studied for formulation of Boswellia serata capsule.
- Based on the performance such as hardness test, friability study, dispersion time, disintegration time & invitro dissolution study all the tests taking to consideration Boswellia serata capsule were evaluated.
- Based on the foregoing conclusion and result emulsifier were used characterized as follows: -**TPGS > QUILAJA> TWEEN 80**
- The optimized formula for boswellia serrata, containing 7% tpgs as an emulsifier, which satisfies the basic official requirements of solubility enhancement. drug contain 88%, 3% tween 80 and 2% hpmc.
- Quilaja & peg 4000 are found to less effective than tpgs and which does not satisfy the basic official requirements of solubility enhancement of the drug.

4. CONCLUSION

- From the present study, capsule of boswellia serata is found to more promising formulation, resulting a faster disintegration and rapid dissolution. Which is achieved by employing suitable emulsifier and solubilizing agent.
- These suggest that enhancement of solubility of capsule formulation are developed in this work hence it may be alternative to the conventional formulation of boswellia serata.
- Capsule of boswellia serata was prepared by the solid dispersion and solvent evaporation using, tween 80 and tpgs as emulsifiers. By using tpgs as potent emulsifier the capsule showing acceptable solubility, disintegration time and in-vitro drug release was significantly improved. So, it concluded that using the tpgs and tween 80 as potent emulsifier, the oral capsule of the boswellia serrata. They would quite effective by give fast onset action which having more solubility and permeability.
- So, the optimized formulation of boswellia serrata having more solubility and permeability.
- Boswellia serata is an anti-inflammatory drug, inhibit 5-lipoxygenase with anti-arthritic effects, which have rapid onset action. It have long duration of the activity it is used for treatment osteoarthritis and asthma etc.
- Oral route always prefers, route of administration for drugs because of the accurate dose, self-medication, low cost hence ease of the administration leading by the high level ofthe patient compliance.so the capsule dosage form is suitable for this formulation.

- To see all the above discussion and result we concluded that the optimized formulationof boswellia serrta having enhance solubility and highly permeability.
- As compare to the control api sample the formulation sample having 50% enhancementof drug release and solubility.
- To Increase The Further More Solubility And Drug Release The Experiment Work Under.

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