FORMULATION AND EVALUATION OF TASTE MASKED ROXITHROMYCIN SUSPENSION AND ITS COMPARATIVE EVALUATION WITH MARKETED SAMPLE

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Submitted by

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This is to certify that the dissertation entitled ***"Formulation and Evaluation of taste masked Roxithromycin suspension and its comparative evaluation with marketed sample"*** is submitted by the candidate bearing **Register No. 26108308** for **The Tamil Nadu Dr. M.G.R. Medical University** examinations.

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CERTIFICATE

This is to certify that the dissertation entitled **"Formulation and Evaluation of taste masked Roxithromycin suspension and its comparative evaluation with marketed sample"** submitted by the candidate bearing Reg. No. 26108308 in partial fulfillment of the requirements for the award of the degree of **MASTER OF PHARMACY** in **PHARMACEUTICS** by The Tamil Nadu Dr.M.G.R. Medical University is a bonafide work done by him during the academic year 2011-2012.

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LIST OF ABBREVIATIONS

HPMC	Hydroxy Propyl Methyl Cellulose
EPH	Ephedrine Hydrochloride
CPM	Chlorpheniramine Maleate
API	Active Pharmaceutical Ingredient
DM	Demineralised
S	Suspension
mL	Millilitre
TSA	Tryptone Soya Agar Medium
SCA	Sabouroud's Chloramphenicol Agar Medium
CFU	Colony forming units
C	Centigrade
RH	Relative Humidity
ICH	International conference on Harmonisation
mcg	Microgram
Cps	Centipoise
F	Sedimentation Volume

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Introduction

INTRODUCTION

SUSPENSION

It may be defined as a coarse dispersion of finely subdivided insoluble solid drug suspended in a suitable liquid (usually aqueous) medium.[1]

It is a heterogeneous system consisting of a solid disperses in a solid, liquid or gas.[2]

It is a biphasic preparations particle of one or more solids basically it may be flocculated or deflocculated.[3]

ORAL SUSPENSION

It contains one or more active ingredients suspended in a suitable vehicle.Suspended solids may slowly separate on keeping but are easily redispersed. It should be packed in wide mouth bottles.[4]

ADVANTAGES OF ORAL SUSPENSIONS

It is a better means of administration than of solid dosage forms such as tablet, capsules especially when swallowing is difficult.[1]

1. It is an ideal dosage form for infants and old patients because of easy administration.[5]
2. It contains sub-divided solid particles, surface area is large and this is taken advantage of drugs which are adsorptive.[1]
3. Suspensions are chemically more stable than solutions.[5]

DESIRABLE PROPERTIES OF SUSPENSIONS [1]

1. It should not be rapid settling of suspended particles.
2. The particles do settle they must not form a hard cake at the bottom of the container.
3. It should be redispersible into uniform mixture when shaken.
4. A suspension should be easily pourable.
5. The colour and odour should be acceptable and pleasing for oral and external uses.

6. Appropriate preservatives should be incorporated in order to minimize the microbial contamination.[5]

PROBLEMS OF SUSPENSIONS [4]

1. Wetting of disperse phase.
2. Settling of disperse phase and resuspendibility of settled matter.
3. Particle – particle interactions leads to particle size growth or caking.

To formulate a suspension the above problems have to be overcome.

FORMULATION OF SUSPENSIONS [4]

In designing a suspension formula, a number of factors must be kept in sight. First of all a decision has to be taken whether a flocculated or non-flocculated system has to be evolved. Secondly, it's important to ensure that the disperse phase particles are well dispersing in the continuous phase. Then finally the decision have to be taken about suspending agents, dispersants, organoleptic additives and preservatives is required to produce satisfactory suspension.

The choice of an appropriate suspending agent depends upon the use of products, facilities for preparation and the duration of product storage.

PHARMACEUTICAL APPLICATIONS OF SUSPENSION [1]

1. FOR ORAL USE

- A suspension provides convenient means of administering an insoluble drugs as compare to tablets or capsules as far as swallowing is concerned.
- Suspensions are fast acting because of more surface area. Eg. $CaCO_3$
- Insoluble derivatives of drugs are often used to reduce the unpleasant taste. Eg . Chloramphenicol palmitate
- Insoluble drugs which are susceptible to hydrolysis are dispensed as dry syrups and are reconstituted with water at the time of use. Eg. Ampicillin Dry syrup

B) FOR EXTERNAL USE

- A number of lotions are of suspension type. Eg.Calamine lotion
- Semisolid Suspensions are paste. Eg. Tooth paste

C) FOR INJECTIONS

- Insoluble drugs which are susceptible to hydrolysis are dispersed as sterile powders in vials. At the time of their use they are reconstituted with sterile water injection. Eg. Penicillin injection.

EVALUATION OF SUSPENSIONS [4]

A number of procedures have been suggested in the past for evaluating the physical stability of suspensions. Some of these are empirical in the sense that they have no mathematical base. Some methods currently being used are so drastic that they destroy the structure of suspension. The methods used may be categorized as

- Sedimentation methods
- Rheological methods
- Electro kinetic methods
- Micrometric methods

TASTE MASKING

Swallowing tablet is a problem for many patients particularly for children and geriatric patients because of when the tablets are large. So prefer oral dosage form. Certain medicaments have an unpleasant taste in the throat when they after orally administered. So some agents are disclosed which when incorporated in the composition mask these bitter taste.[6]

The conventional oral dosage forms possess sustained release anti – tussive characteristics.

Microcapsules are formulated into chewable taste masked oral tablets or capsules the formulation provide for immediate rapid release in the stomach. The meth acrylic acid copolymer can be a copolymer of polymethacrylic acid and acrylic

acid esters. These polymers coating should be used for immediate release characteristics in microcapsule techniques.[7]

Many drugs containing amine or amide groups or salts there of often have a strong bitter taste. Taste masking techniques using various sweeteners, amino acids, flavours & adsorbents have been unsuccessful in masking the taste. In most coating techniques don't have an acceptable in-vivo drug releasing mechanism.

Cat ion exchange resins have been used to adsorb amine drugs for sustained release action & taste masking .The widely used cat ion – exchange resins are poly sulfonic acid & poly carboxylic acid polymers[3].

A variety of delivery systems are being developed for different routes of administrations like oral, parenteral, nasal & transdermal, The oral route remain attractive for drug delivery because this mode of administration is an easy, convenient, noninvasive & familiar method of drug delivery oral dosage forms are designed according to the nature of the drug.[8]

The common oral dosage forms include liquid mixtures like tablets, capsules & liquid filled capsules. The solid dosage forms are further modified depending on the therapeutic action desired like controlled, extended, or delayed release.

Patients at the extremes of age, such as children and the elderly often experienced difficulty in swallowing solid dosage forms such as solutions, emulsions & suspensions. These dosage forms usually lead to perceptible exposure of the active drug ingredient to the taste buds, which is a very serious problem when the drag has an extremely unpleasant.[9]

Conventional taste masking techniques such as sweeteners, amino acids, flavoring agents are often unsuccessful in masking the taste of the highly bitter drugs like quinine, barberin, antibiotics like ofloxacin & clarithromycin.

Taste masking is a major problem when the drugs are extremely unpleasant this problem is not restricted to the liquid oral composition like solutions, dry syrup & suspensions but may also be encountered during the formulation of chewable tablets where in these dosage forms usually lead to perceptible exposure of active ingredient to taste buds. Depending on the type of dosage form various

methods have been employed to overcome the unpleasant taste and bitterness of the drug.

Various method for taste masking have been tried earlier which include use of ion exchange resins, complexation of bitter drugs with pharmaceutically acceptable recipients and coating of drugs by lipids using a various polymeric materials. The coating is the most widely used technique for taste masking. Coating of the active ingredient can be done by any of the techniques known in the art like microencapsulation.

The use of ion exchange resins to absorb drugs containing amino groups for taste masking has found limited applicability in masking the taste of highly bitter drugs, and also where the drugs is to be dispersed in a liquid oral composition for long duration of time.

Another technique is mouth disintegrating tablet. In this method, disintegrate in oral cavity with saliva in 15 sec to 60 sec, without need of water and should have pleasant mouth feel.[10]

The two methods were followed for the formulation of mouth disintegrating tablets.

- By addition of sweeteners and disintegrants.
- Mass extrusion technique.

These taste masking formulations frequently are flavoured such as with fruit or mint flavours, usually for purposes of masking an unpleasant taste caused by the presence of a dissolved or suspended pharmacologically active substance. A pleasant taste is particularly important when the formulation is intended for ingestion by children. The typical flavours which are commonly used in formulations. The important flavours such as grape, cirus, peach, strawberry, peppermint and many other flavors.

In these formulations, non- sugar based artificial sweetening agents like sucralose & saccharin are used.

Typically suitable pharmaceutically acceptable solvents and or carriers systems include water, alcohols & glycerin are used.[11]

Suitable buffering systems are also used in the formulations. That is citric acid & phosphoric acid buffer systems. The citric acid buffer system preferably contains sodium citrate in combination with citric acid.

In these formulations, P^H range is about 4.5 to 6.5 preferably 5.5 is maintained.

Suitable thickening agents are used in these taste masking formulations that is xanthangum, guargum, gelatin, taragum, tracaganth gum and many others.[12]

In this taste masking formulations, to prevent microbial contamination, preservatives like sodium benzoate (0.1 to 0.2%) or benzoic acid is used.

Stabilizers also be incorporated into the taste masking formulations in the amounts of about 0.01 to 5% preferably about 0.25%.

TECHNIQUES EMPLOYED FOR TASTE MASKING

The methods commonly employed for achieving effective taste masking include various physical and chemical methods that prevent the drug substance from interaction with the taste buds.

A) Use of Flavor Enhancers

The materials for taste masking purpose have often been classified depending upon the basic taste that is masked.[13] Flavoring and perfuming agents can be obtained from either natural or synthetic sources. Natural products include fruit juices, synthetic products like aromatic oils such as peppermint oil and lemon oil, herbs, spices and distilled fractions. They are available as concentrated extracts, alcoholic or aqueous solutions, syrups or spirit.[14]Apart from these conventional materials many compositions have been found to show effective taste masking abilities with improved flavor such as alkaline earth oxide, alkaline earth hydroxide or an alkaline hydroxide.[15] Another composition includes phosphorylated amino acid such as phosphotyrosine, phosphoserine, and phosphothreonine and mixtures thereof.[16] Anethole effectively masked bitter taste as well as the after taste of zinc,

which is use in treating the common cold[17]. Clove oil and calcium carbonate which has been found to be particularly useful to mask the unpalatable active in formulation which are intended to be chewed or dissolve in mouth prior to ingestion in solution.[18]

B) Applying Polymer Coatings

Coating of drugs using a suitable polymer offer an excellent method of concealing the drug from the taste buds. The coated composition may be incorporated into much number of pharmaceutical formulations, including chewable tablet, effervescent tablets, powder and liquid dispersion.[19-21]

Multiple encapsulated flavour delivery systems has been developed which is useful in chewing gum, pharmaceutical preparations as well as other food products.[22]

C) Complexation and Adsorption Approaches[23]

Complexation with ion exchange Resins and Polymers

Cat ion-exchange resin CRP 244 and anion exchange ion were used to adsorb ester drugs for both masking of bitter taste and achieving sustained release action. The types of ion exchanges resins that have been successfully used to mask the taste of bitter drugs include amberlite IRP 88 (an acrylic potassium resin), amberlite IRP 64 (a polystyrene sulphonate) and amberlite IRP 64 (a carboxylate form of the methapyrilene, dextromethrophan, ephedrine and pseudoephedrine) were masked by first forming adsorbates with polymethacrylic acid ion exchange resin followed by coating of resin complex with 4:1 mixture of ethyl cellulose and hydroxy propyl methyl cellulose (HPMC)polymers.

Prepared high potency adsorbents of methapyrilene, dextromethophan, ephedrine, pseudoephedrine by column procedures using a polymethacrylic acid ion exchange resin. Taste evaluation of the adsorbents showed a significant reduction in the bitterness of the drugs. Coating adsorbent particles with 4:1 ethyl cellulose-HPMC mixture reduced the bitterness further. Taste coverage was maintained after

incorporation of the coated adsorbent in to chewable tablets. Strong acid cat ion resins (sulfonated styrene divinyl benzene copolymer product) can be used for masking the taste of basic drugs.[23] Polystyrene matrix cat ion exchange resins have been used to mask the bitter taste of chlorpheniramine malate, ephedrine hydrochloride and diphenhydramine hydrochloride.[24] Extreme bitterness of quinolones has been achieved by ion exchange resin such as methacrylic acid polymer cross linked with divinylbenzene.[25]

DRUG RESIN COMPLEXES

When an ionizable drug reacts with a suitable ion exchange resin, the drug-resin complex formed is known as a drug resinate. Since the drug resinate is insoluble, it has virtually no taste, so that even very bitter drugs lose their taste when converted into a drug resinate with the correct selection of the ion exchange resin. The drug resinate can be made sufficiently stable that it dose not break down in the mouth so that the patient does not feel the taste of drug when it is swallowed. However, when the drug resinate come in contact with gastrointestinal fluids, usually the acid of the stomach. The complex is broken down quickly and completely. The drug is released from resinate directly into the solution and then absorbed in the gastrointestinal tract without being absorbed.

D) Formulation of Inclusion Complex with Beta Cyclodextrin Derivatives[12]

Cyclodextrin are cyclic oligomers of glucose. They form inclusion complexes with any drug whose molecules can fit to the lipophile seeking cavities of the cyclodextrin molecule. The resulting complexes can marked improve the coating with suitable lipids, such as palmitic or stearic acid, glyceryl tripalmitate, glyceryl tristearate or a mixed acid ester triglyceride and stearyl alcohol.[26,27]

E) Wax Embedding of Drugs[12]

Taste masked by wax embedded granules of ephedrine hydrochloride, chloropheniramine maleate and Diphenhydramine hydrochloride were prepared in stearic acid and other waxes.

F) Other Techniques

These include solubility-limiting methods incorporation of drugs in vesicles and liposome and chemical modification.[28,29] The solubility limiting method can be applied to a number of drugs whose taste profiles are dependent on aqueous solubility.

Chemical modification such as derivatization or lipophillic counter ion selection may be an effective method for reducing aqueous solubility and taste. Erythromycin monohydrate, a bitter tasting drug with a solubility of 2 mg/ml is chemically converted into erythromycin ethyl succinate, the aqueous solubility is reduced to the <50mcg/ml.This form is tasteless and can be administrated as a chewable tablet. Incorporation of drugs into Vesicles or liposomes is although an ideal technique. Yet a challenge to formulate without altering the regulatory status of the product (in-vitro dissolution kinetics, physical or chemical stability or bioavailability). [28]

Anesthetizing agent like sodium phenolate, which numb the taste buds sufficiently within 4-5 seconds is helpful in inhibiting the perception of the formulation[30]. Substances like lipids, carbohydrate, lecithin, gelatin and polyamines has been effectively used for taste masking of drugs.[31]

Another novel technique employing mulitiple emulsions has also been reported. By dissolving drug in the inner aqueous phase of w/o/w emulsion under condition of good shelf stability, the formulation is designed to release drug through oil phase in the presence of gastric fluid.[32]

In one of the method drugs with bitter taste are combined with non-ionic surfactants to form composites by hydrophobic interactions resulting in taste masking.[33]

TECHNIQUES EMPLOYED FOR TASTE MASKING OF DIFFERENT DOSAGE FORMS[34]

The drug i.e. the active pharmaceutical ingredient is finally formulated in a suitable dosage form such as tablet, powder, liquid, etc.

(i) Tablets

Most of the tablets can be effectively masked for their taste by applying inert polymer coatings that prevent the interaction of the drug substances with the taste buds. Nevertheless, attempts have been made time and again by several workers to investigate and explore the use of newer materials in bad taste abatement and good taste enhancement.

(ii) Granules / powders

Granules for reconstituting as liquids (e.g. sachets, sprinkle capsules & powder) hold a high share of pediatric and geriatric market. A large number of patients on the topic highlight the significance of the same. Thus taste masking of granules becomes an important priority in product development and varied technologies and methodologies.

(iii) Liquids

They present major challenges in taste majority of pediatric preparation are syrups and suspensions although, the aforementioned methodologies have also had been used for improving liquid taste and few patents in this area are worth mentioning.

Literature Review

LITERATURE REVIEW

01. Akemi N et al. [35] developed a method of taste of clarithromycin using a spray congealing technique using glyceryl monostearate and amino alkyl methacrylate copolymer showed that in ratio 3:6:1 for clarithromycin glyceryl monostearate and aminoalkyl methacrylate copolymer showed better result.

02. Hiroyo S et al. [36] studied taste making of bitter drug powder of indelozagine hydrochloride by mixture comprising hydrogenated on and surfactant in fluidized bed dryer using the side spray method showed that by heat treatment the coated particles at a room temperature above the melting point of a surfactant in the coated layer cause remarkable increase in dissolution rate.

03. Geeta Rao CG et al. [37] formulated taste masked oral suspension by complexation technique using ion-exchange resins. The suspension was evaluated and release studies showed complete drug release within 20 minutes stability studies indicated no appreciable change in suspension.

04. Kishimoto et al. [38] used mannitol and lactose in different weight ratios (1:1.5-1:5) as coating materials for masking bitter taste of solid drug preparations.

05. Yajima et al. [39] described in their patent with a composition comprising of a drug with unpleasant taste of polymer solution and D-crystals of monoglycerides. Eudragit-E (100g), monoglyceride (600g) and then erythromycin (300g) were added to the mixture to obtain a powder to give taste masked granules of erythromycin.

06. Danielson et al. [40] invented a dosage form comprising a granules containing the histamine receptor antagonist which are provided with taste masking comprising a water insoluble, water permeable methacrylate ester copolymer in which the coating is applied to the granules in an amount which provides a taste masking effect for a relatively short period during which the composition is being chewed by the patient but which allows substantially immediate release of the histamine receptor antagonist after the composition has been chewed and ingested.

07. Kumar et al. [41] provided a means and method for manufacturing palatable drug granules using a copolymer having least one free carboxyl group and poly vinyl pyrolidone.

08. Meyer et al. [42] used Prolamine as single coating in weight ratio 5% to 100% relative to active substance being coated result in the production of liquid suspension which effectively masked the taste of orally administered drugs which are extremely bitter. Prolamine coating is effective in masking the taste of antibiotics, vitamins. analgesics,enzymes and hormones.

09. Nakona et al. [43] masked the bitter taste of vitamin B1 derivatives such as dicethimines by formulating with methanol and or poly oxyethylene, poly oxy propylene for formulating oral liquids.

10. Osugi et al. [44] subjected in their invention oral liquids containing Diclofenac and its salts to heat treatment in the presence of glycine, said there of to mask the bitter taste and to prevent the irritation of the throat upon oral administration.

11. Morella et al. [45] invented a liquid suspension of microcapsules taste masked as a function of a polymer coating and the pH of suspended medium at which pharmaceutically active ingredients remain substantially insoluble.

12. Swaminathan et al. [46] developed pharmaceutically composition comprising polyhydric alcohol based carrier to mask the bitter taste of drug.

13. Yu et al. [47,48] invented a liquid composition comprising a pharmaceutically active medicament coated with a taste masking effective polymer blend of dimethylaminoethyl methacrylate and natural methacrylic acid aster and a cellulose ester in an aqueous vehicle.

14. Cuna et al. [49] prepared micro encapsules of cefuroxime axetil with various cellulosic polymers having a pH dependent solubility; CAT, BPMCP-55 and UPMCP-50, with the final aim to mask its taste while assuring its release in the intestinal cavity.

15. Kato et al. [50] studied the low melting point substances for masking bitter taste of the drug beef tallow was mixed with micropulverized active ingredients and the mixture was nozzle sprayed to form coated spheres having homogenous particle size.

16. Maccari et al. [51] conducted a special study to assess the bioavailability of a Flucoxacillin preparation microencapsulated for taste abatement with 17 % ethyl cellulose made up as a granular product for extemporaneous resuspension when compared to commercially available flucoxacillin preparations.

17. Udea et al. [52] described a novel microencpsulation process combined with the wet spherical agglomeration technique by using modified phase separation method in order to mask the bitter taste of drug.

18. Yekta Ozer et al. [53] mictoencapsulated Beclamide in order to mask the bitter taste by a simple co-acervation method using-gelatin.

19. Borodkin et al. [54] prepared high potency adsorbates of Methapyrilene, Dextromethorphan, Ephedrine, Pseudoephedrine by column procedures using a polymethacrylic acid ion exchange resin.

20. Yoshimi et al. [55] studied the influence of heat treatment on dissolutions and masking degree of bitter taste for novel fine granule system.

21. Cuna M et al. [56] disclosed microeneapsulation of highly bitter drug Cefurorxime Axetil for taste masking by using different polymeric materials like cellulose acetate trimellitate, HPMC-50, HPMCP-55 with the final aim to mask the taste and assuring its release in the intestinal cavity.

22. Alonso et al. [57] developed the encapsulation of Cefuroxime Axetil, a highly bitter drug, in pH sensitive acrylic microspheres in order to formulate a suspension dosage form is described. The acrylic polymers used were Eudragit-E, Eudragit RL – l00, Eudragit L-100, 55. The cationic polymer Eudragit-E showed a negative interaction with cefuroxime axetil. The enteric polymer Eudragit L-100 and 55 showed a favourable release in alkaline pH.

23. Dantzig et al.[58] showed the cefuroxime axetil is hydrolyzed to cefuroxime in the intestinal lumen by the esterases reducing the cefuroxine axetil concentration in the lumen and resulting in reduced absorption leading to low bioavailability of cefurokime axetil in humans. Cefuroxime axetil already has a low bioavailablability of 32-50% and hence further reduction in the bioavailability due to the formulation aspects should be minimized.

24. Patent Application WO 00/56266 [59] disclosed the use of high viscosity swellable polymer carbomer in combination with film forming polymethacrylates and channelising agents for taste masking of bitter drugs. The addition of the water swellable polymer aids in the fast release of the active ingredient in the gastric media.

25. Patent Application 100 00/76479 [60] disclosed a taste masking composition, using a combination of two enteric polymers comprising a methacrylic acid copolymer comprising a methacrylic acid copolymer and a phthalate polymers is disclosed. The enteric polymers as disclosed in the patent are known to release the active ingredient in the alkaline pH where the polymers are soluble.

26. British Patent 2081092 [61] disclosed a lipid coating for the purpose of taste masking. It was however found that wax coating resulted in poor dissolution of the active ingredients in the alimentary tract. Further the patent discloses a technique to over come this problem by mixing the waxes with a water swellable polymer. The use of water swellable polymer referred to in the patent makes it less appropriate for the liquid orals like suspension and dry syrup.

27. US Patent No. 5,286,489 [62] described a porous drug polymer matrix formed by admixing a bitter tasting active ingredient and a methacrylic ester copolymer in at least a 1:1 weight ratio of active ingredient to copolymer, effective to mask the taste of the drug.

28. Patent Applications WO 02/072111 [63] disclosed a taste masked pharmaceutical suspension of telithromycin. For different coating agents Novata-AB, Eudragit E-100, glycerol monostearate and talc M 10 are employed and at least three successive layers of coating are essential to taste mask telithromycin. The coated grranules as disclosed could further be formulated as dry syrup, which is reconstituted as a suspension.

29. US Patent.No.4,865,851 [64] disclosed for taste masking highly bitter lacetoxy ethyl ester of Cefuroxime in particular form being coated with an integral coating of lipid or a mixture of lipids, which serves to mask the bitter taste.

30. US Patent Application 2003-028025[65] disclosed taste masked composition of gatifloxacin suitable for use in oral dosage forms, particularly for pediatric formulations. A crystalline co-precipitate of gatifloxain and one or both of stearic acid and palmitic acid is used to effectively mask the bitter taste of gatifloxacin in the mouth and in a aqueous suspension through a full dosage cycle of fourteen days.

31. US Patent No.5,635, 200[66] disclosed a taste masked preparation of bitter drug ranitidine by a lipid coating and dispersion of these coated particles in the non-aqueous medium.

32. US Patent No.4808, 411[67] disclosed a taste masked composition comprising 75-95% of erythromycin and about 5 to 75% of carbomer where the drug and carbomer are held together by ionic interactions between erythromycin and carbomer. The complex is further coated with a functional polymer, HPMC, phthalate to mask the preparation palatable complexing alone is not sufficient enough to mask taste. Coating with functions polymers is required to attain desired palatability.

33. US Patent 6514492[68] disclosed the use of exchange resin AMBERLITE. RTM. IRP 69 for taste masking of quinolone derivatives there by eliminating the extreme bitterness of the quinolones in oral liquid formulation.

34. Patent Application wo 01/52848[69] disclosd a taste masked oral formulation linezolid which can be formulated as a suspension a fast disintegrating, effervescent or chewable tablet, by microencapsulating the antibiotic by solvent evaporation of ethyl cellulose with an optimal seal coat of shellac and further coating the particles by functional polymer Eudragit L-30 D.

35. Patent Application wo 01/58449[70] disclosed the water dispersible powder and tablets of paroxetine for the immediate release of the drug and a taste masking agent comprising of the methacrylic acid copolymer. The taste masked composition was obtained by spray drying of paroxetine and the polymer.

Aim, Objective and plan of work

AIM, OBJECTIVE AND PLAN OF WORK

AIM OF THE PRESENT STUDY

Aim of the present study is development and evaluation of taste masked Roxithromycin oral suspension.

OBJECTIVE OF THE PRESENT STUDY

The objective of the present study is to mask the bitter taste of a candidate drug of Roxithromycin for suspension.

Oral suspensions are suitable for those people who cannot swallow the tablets or in case of pediatrics. In such cases oral suspension is the choice. At the same time the candidate drug is very bitter in taste so its taste should be masked prior to dosage form development.

Desired characteristics of final product: [1]

It should have an acceptable taste and appearance.

- The taste, pH,Viscosity, Colour and flavour of the oral suspension must be stable throughout the shelf life.
- It should be free from microorganisms.

PLAN OF THE PRESENT STUDY

The study was planned to carry out as follows

- Literature survey
- Preformulation study
- Physical characterization of active-solubility
- Taste masking of drug by Drug-Resin Complexation
- Preparation of suspension.

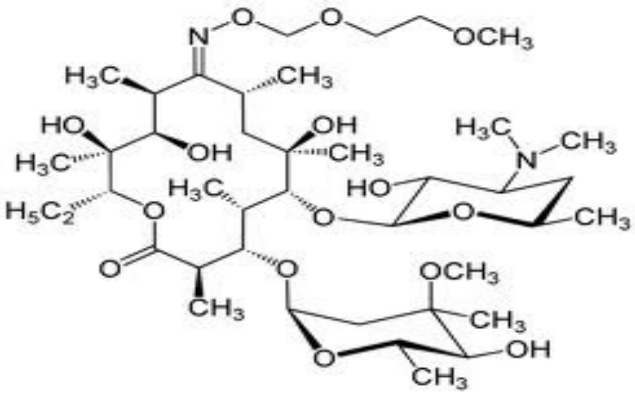
- Evaluation of Suspension
    - Taste
    - pH
    - Viscosity
    - Sedimentation volume
    - Assay
    - Dissolution study
    - Microbial testing
    - Stability testing

Profiles

DRUG PROFILE[71, 72]

Drug name : Roxithromycin

Structural formula



Chemical name : (3*R*,4*S*,5*S*,6*R*,7*R*,9*R*,11*S*,12*R*,13*S*,14*R*)-6-[(2*S*,3*R*,4*S*,6*R*)-4-d- 3-hydroxy-6-methyloxan-2-yl]oxy-14-ethyl-7,12,13-trihydroxy-4-(2*R*,4*R*,5*S*,6*S*)-5-hydroxy-4-methoxy-4,6-dimethyloxan-2-yl]oxy-10-(2-methoxyethoxymethoxyimino)-3,5,7,9,11,13-hexamethyl-1-oxacyclotetradecan-2-one

Emperical formula : $C_{41}H_{76}N_2O_{15}$

Molecular weight : 837.05

Functional category : Semi-synthetic macrolide antibiotic

TYPICAL PROPERTIES

Description : White crystalline powder.

Melting Point : 115 - 120^{0}C

Solubility : Freely soluble in ethanol and in acetone,
Soluble in methanol, sparingly soluble acetonitrile,
Practically insoluble in water.

Contra indication : Hypersensitivity to Roxithromycin or other macrolides

Adverse effect : Blood disorders, Immune system disorders,Nervous system disorders, Cardiac disorders, gastrointestinal disorders, Hepatobiliary disorders, General disorders.

Administration : 150 mg every 12 hours before food.

PHARMACOKINETICS

- Bioavailability is almost 100%
- Peak plasma concentration is achieved in 2 hours after a dose of 150 mg by mouth.
- The plasma half-life ranges from 12 hours.
- About 96 % bound to alpha-1-acid glycoprotein.
- Partly metabolised in the liver
- More than 50 % of the dose being excreted in the faeces as unchanged parent drug. The remainder is excreted in the urine
- The average elimination half-life is 10.5 hours, but may be prolonged in children, in patients with hepatic impairment (25 hours), in the elderly (27 hours) and in the renal impaired (18 hours).
- Transmission to the cerebrospinal fluid is slow.

THERAPEUTIC USES

- To treat respiratory tract, urinary and soft tissue infections
- It also possess anti malarial activity.

DISEASE PROFILE [73]

Roxithromycin is used to treat various infections caused by bacteria.

- Acute Pharyngitis (sore throat and discomfort when swallowing.
- Tonsillitis.
- Sinusitis.
- Acute bronchitis (infection of the bronchi causing coughing).
- Pneumonia (lung infection characterised by fever, malaise, headache).
- Skin and soft tissue infections.
- Non gonococcal urethritis.
- Impetigo (bacterial infection causing sores on the skin).

PHARYNGITIS

Pharyngitis is a sore throat caused by inflammation of the back of the throat. Pharyngitis or sore throat is discomfort, pain, or scratchiness in the throat. It often makes it painful to swallow.

CAUSES

Most sore throats are caused by viruses, although a few are due to bacterial infections. Bacteria or a virus that are spread in the air when someone sneezes or coughs, or you can transfer the organisms to your mouth or nose by touching a surface with germs on them. Viruses that can cause sore throat include the common cold, the flu, and mononucleosis (often called "mono"). Bacteria like Group A *streptococcus* (commonly known as strep throat) can also cause Pharyngitis.

SIGNS AND SYMPTOMS

The symptoms that accompany a sore throat can vary, depending on what the underling illness is,

- **Sore throat with cold**

- Sneezing
- Cough

- A low fever (less than 102 °F)
- Mild headache

➢ **Sore throat with flu**

- Fatigue
- Body aches
- Chills
- Fever higher than 102 °F

➢ **Sore throat with mononucleosis**

- Enlarged lymph nodes in neck and armpits
- Swollen tonsils
- Headache
- Loss of appetite
- Swollen spleen
- Liver inflammation

RISK FACTORS

Risk factors for Pharyngitis include

- Cold and flu seasons
- Having close contact with someone who has a sore throat or cold
- Smoking or exposure to second hand smoke
- Frequent sinus infections
- Allergies

DIAGNOSIS

- Checking the temperature
- Examine throat, sinuses, ears, nose, lungs, and neck, including feeling for swollen lymph nodes that may indicate strep throat. May take a throat culture or do a rapid strep test by taking a swab from throat.
- A blood test may be done to check for mononucleosis.

PREVENTIVE CARE

- Avoid kissing or sharing cups and eating utensils with anyone who has a sore throat, a cold, flu, mononucleosis, or bacterial infection.
- Wash your hands frequently.
- Don't smoke, and avoid exposure to second hand smoke.
- Use a humidifier if the air in your home is dry.

TREATMENT APPROACH

- Gargling with salt water.
- Counter pain reliever such as acetaminophen (Tylenol) or ibuprofen (Advil, Motrin).

LIFESTYLE

- Rest
- Fluid intake. Water and warm broths are better than soft drinks.
- Avoid drinking alcohol.
- Gargle several times per day with ½ teaspoonful of salt in a glass of warm water
- Try throat lozenges (do not give to a child under 3 years old due to choking hazard).

MEDICATIONS

If patient have sore throat due to bacterial infection, **Roxithromycin** is the most commonly prescribed drug.

EXCIPIENT PROFILE

CITRIC ACID MONOHYDRATE[74]

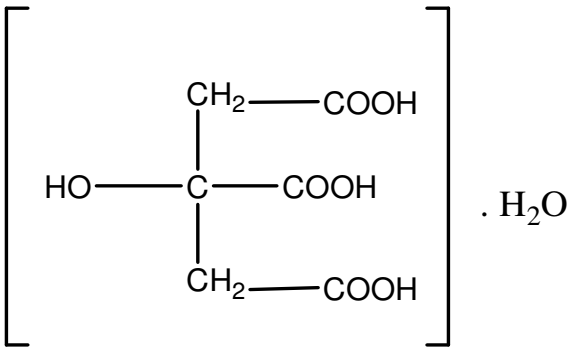
Synonym : Hydroxypropane – 1, 2,3-tricarboxylic acid monohydrate.

Chemical name : Hydroxy-1, 2,3-propanetricarboxylic acid monohydrate.

Emperical formula : $C_6H_8O_7.H_2O$

Molecular weight : 210.14

Structural formula :



Description : Colourless translucent crystals. White crystalline, effervescent powder.Odorless, strong acidic taste, Crystal structure is ortho rombic.

TYPICAL PROPERTIES

pH : 2.2 (1% w/v aqueous solution)

Density : 1.542 g/cm^3

Melting point : 100^0C (Softens at 75^0C)

Solubility : Soluble in 1.5 parts of ethanol (95%) and 1 in less than 1parts of H_2O, sparingly soluble in ether.

Viscosity : 6.5Mpas for a 50% w/v aqueous solution at 25^0C

Incompatibilities : It incompatibles with potassium tartrate, alkali and alkaline earth carbonates, and bicarbonates, acetates and sulfides, sucrose may crystallize from syrups in the presence of citric acid.

Functional category

- Buffering agent
- Chelating agent
- Acidifying agent
- Flavouring agent
- Flavour enchancer

Applications:

- It is widely used in pharmaceuticals, formulations and food products primarily adjust the pH of the solution.
- It is available as monohydrate and anhydrous material.
- Citric acid monohydrate : Preparation of effervescent granules
- Citric acid anhydrous : Preparation of effervescent tablets.

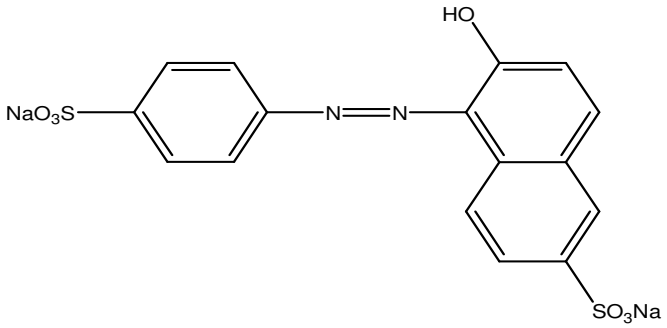
SUNSET YELLOW FCF[74]

Synonym : 6-Hydroxy-5-[C4-sulfopheny1) azo]-2-napthalene sulfonic acid disodium salt; 1-p-sulfophenyl azo-2-napthanol-6-sufonicacid disodium salt; yellow oranges.

Empirical formula : $C_{16}H_{10}N_2Na_2O_7S_2$

Molecular weight : 452.37

Structural formula :



Appearance : Reddish yellow powder, aqueous solutions are bright orange coloured.

Solubility :

Table-1: Solubility Profile

SOLVENT	SOLUBILITY AT 25° C UNLESS OTHERWISE STATED
Acetone	1 in 38.5
Ethanol (75%)	1 in 333
Glycerin	1 in 5
Propylene glycol	1 in 45.5
Propylene (50%)	1 in 5
Water	1 in 5.3 at 2°c 1 in 5.3 at 25°c

Incompatabilities : Poorly compatible with citric acid, saccharine solutions and saturatred sodium bicarbonate solutions.
Incompatible with ascorbic acid, gelatin and glucose. It's a mono azo dye.

pH : 1.3

Applications

- The primary purpose of colouring agent is too visually after the appearance of a medicinal product by imparting a definite colour.
- The use of colour in medicinal products is conjugation with other factors. Such as shape and packing, additionally serves to reinforce brand image and identity.
- It can also serve to introduce a uniformity of appearance to a product.
- Dyes (Soluble in H_2O)
- Pigments (Insoluble in H_2O)

METHYL PARABEN[74]

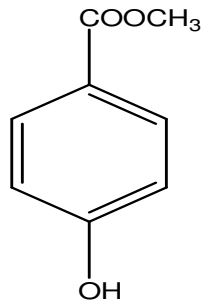
Synonym : 4 – hydroxyl benzoic acid methyl ester; Methyl Chemosept; Methyl p – hydroxybenzonate; Methyl parahydroxybenzonate; Methyl Para sept.

Chemical name : Methyl 4 – hydroxy benzoate

Empirical formula : $C_8H_8O_3$

Molecular weight : 152.15

Structural formula :



Functional Category : Antimicrobial preservative

Description : Colourless crystals, White crystalline powder Odourless, Slight burning taste

Incompatibilites : Antimicrobial activity of methyl paraben and other paraben is considerably reduced in the presence of non-ionic surfactants (Polysorbate 80).

Incompatibile with other substances such as bentonite, Magnesium trisilicate, talc, tracaganth, sodium alginate, essential oils, sorbital and atropine.

Applications : Antimicrobical preservative in cosmetics, food products, pharmaceutical formulations.

PROPYLENE GLYCOL[74]

Synonym : 1, 2- Dihydroxy propane; 2-hydroxy propanol; methyl glycol; propane-1,2-diol

Chemical name : 1, 2-propanediol

Emperical formula : $C_3H_8O_2$

Molecular weight : 76.09

Structural formula : $CH_3CHOHCH_2OH$

Functional Category : Antimicrobial preservative, disinfectant, stabilizer for vitamins, Humectant water miscible co-solvent, plasticizer.

Description : Clear, colourless, viscous, partially colourless liquid with a sweet, slightly acrid taste resembling glycerin.

TYPICAL PROPERTIES

Density : 1.038 g/cm^3 at 50°C

Melting point : -59°c

Boiling point : 188°C

Viscosity : 58.1 mpas at 50°C

Solubility : Miscible with acetone, chloroform, ethanol (95%) glycerin, water. Soluble 1 in 6 parts of ether not miscible with light mineral oil, Dissolve some essential oils.

Incompalbillties : It is incompatible with oxidizing reagents such as Potassium permanganate.

Applications : It is widely used as a solvent, extractant, preservative in a variety of parenteral and non parenteral pharmaceutical formulations.

SODIUM CHLORIDE[74]

Synonym : Common salt; Natural halite; rock salt; salt; sea salt; table salt.

Chemical name : Sodium chloride.

Emperical Formula: NaCl

Molecular Weight : 58.44

Structural Formula: NaCl

Description : White crystalline powder,
Odorless crystals,
It has saline taste,
The crystal lattice is a face Centred cubic structure.

TYPICAL PROPERTIES

pH : 6.7-7.3

Boiling point : 1439°C

Density : 2.17g/cm^3 1.20g/cm^3 for saturated aqueous solution.

Bulk density : 0.93g/cm^3

Tapped density : 1.09g/cm^3

Solubility : Slightly soluble in ethanol,
1 in 2.8 parts soluble in water,
1 in 2.6 parts soluble in water at 100°C

Stability and Storage : Aqueous sodium chloride solutions are stable but may cause the separation of glass particles from certain types of glass container. The solid material is stable and should be stored in a well closed container, in a cool dry place.

Incompatibilities : Aqueous sodium chloride solutions are corrosive to iron. They also react to form precipitate with silver, lead and mercury salts.

Story oxidizing agents liberate chlorine from acidified Solutions of NaCl. The solubility of the antimicrobial preservative methyl paraben is decreased in aqueous NaCl solutions.

Applications

- It is widely used in a variety of parenteral and non parenteral pharmaceutical formulations.
- It is used to control drug release from microcapsules.
- It can used adjust the viscosity of polymer.
- It is used as a lubricant and diluent.

SODIUM BENZOATE[74]

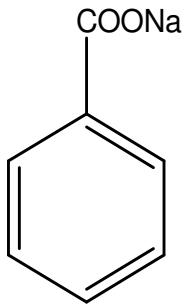
Synonyms : Benzoate of soda; Benzoic acid sodium salt.

Chemical name : Sodium benzoate

Empirical formula : $C_7H_5NaO_2$

Molecular weight : 144.11

Structural formula :



Functional category : Antimicrobial preseravative, Tablet and capsule lubricant.

Description : It occurs as a white granular, crystalline, slightly hygroscopic powder, odorless. It has an unpleasant, sweet and saline taste.

TYPICAL PROPERTIES

pH	:	8.0 (saturated aqueous solution at 25°C)
Density	:	1.15 g/cm^3 at 24°C
Solubility	:	Ethanol (75%) soluble 1 in 75 parts at 25°C)
		Ethanol (70%) soluble 1 in 50 parts at 25°C)

Stability and storage conditions : Aqueous solutions may be sterilized by autoclaving. The bulk material should be stored in a well closed container in a cool, dry place.

Incompatibilities : Incompatible with quaternary compounds, gelatin, ferric salts, calcium salts and salts of heavy metals including silver, lead and mercury.

Non-ionic surfactants may be reduced by interactions with kaolin.

Applications

- Antimicrobial preservative in cosmetics, food and pharmaceuticals.
- It is used in concentration of 0.02-0.5% in oral medicines 0.1-0.5% in cosmetics.
- It may impart an unpleasant flavour to the product.
- It is used as a Tablet lubricant.

SODIUM CITRATE DIHYDRATE [74]

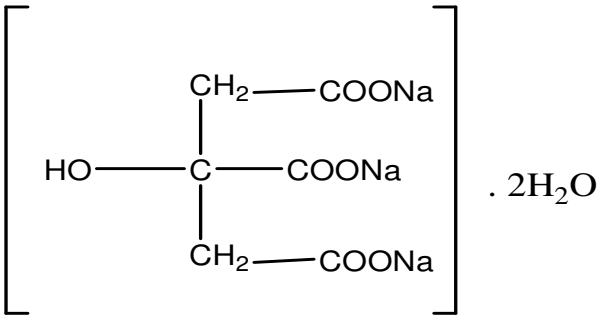
Synonyms : Citric acid trisodium salt; trisodium citrate.

Chemical Name : Trisodium 2-hydroxy propane -1,2,3,-tricarboxylate dihydrate.

Emperical formula : $C_6H_5Na_3O_7.2H_2O$

Molecular weight : 294.10

Structural Formula



Functional Category : Alkalizing agent, Buffering agent, Sequestering agent

Description : Sodium citrate dihydrate consists of odourless, colorless, white crystalline powder with a cooling saline taste, slightly deliquescent in moisture.

TYPICAL PROPERTIES

pH	:	7-9 (5% W/V aqueous solution)
Density	:	1.19g/m^3
Melting Point	:	Converts to the anhydrous form at 150°C

Solubility : Soluble 1 in 1.5 parts of H_2O, 1 in 0.6 parts of Boling water. Practically insoluble in ethanol (95%)

Incompatibilities

- Aqueous solutions are slightly alkaline and will react with acidic substances.
- Calcium and strontium salts will cause precipitation of the corresponding citrates.

Applications

- It is a anhydrous material is widely used in pharmaceutical formulations and food products primarily to adjust the pH of the solutions.
- It is also used as a sequestering agent.

SORBITOL[74]

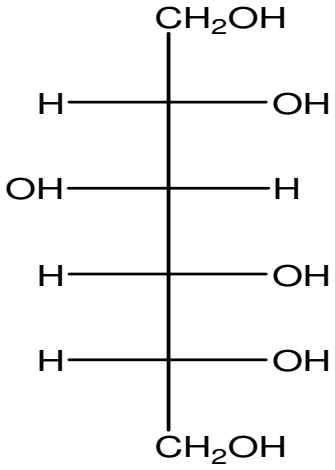
Synonym : 1,2,3,4,5,6,-heanehexol; hydox; neosorb; sorbite; D-sorbitol; sorbitol instant.

Chemical name : D-Glucitol

Empirical formula : $C_6H_{14}O_6$

Molecular weight : 182.17

Structural formula :



Functional category : Humectants,

Plasticizer,

Sweetening agent,

Tablet and capsule diluents.

Description Odourless, white crystalline, hygroscopic powder,Sorbitol has a pleasant cooling ,sweet taste and has a approximately 50-60% of the sweetness of sucrose

TYPICAL PROPERTIES

pH	:	4.5-7.0
Density	:	1.49 g/cm^3
Melting point	:	110-112°C for anhydrous from. 97.7° C for monohydrate. 93°C for metastable monohydrate form.
Solubility	:	Practically insoluble in Chloroform and ether at 25° C. Slightly soluble in Methanol at 25°C Soluble 1 in 0.5 part in Water at 25°C
Incompatibilities	**:**	Sorbitol will form water soluble chelates with many di-and-trivalent metal ions in strongly acidic and alkaline conditions.

Applications

- Sorbitol is widely used as an excipient in pharmaceutical formulations.
- It is also used extensively in cosmetics and food products.
- It is used as a vehicle in sugar free formulations and a stabilizer for a drug (Vitamin and antacid suspensions).

SUCROSE[74]

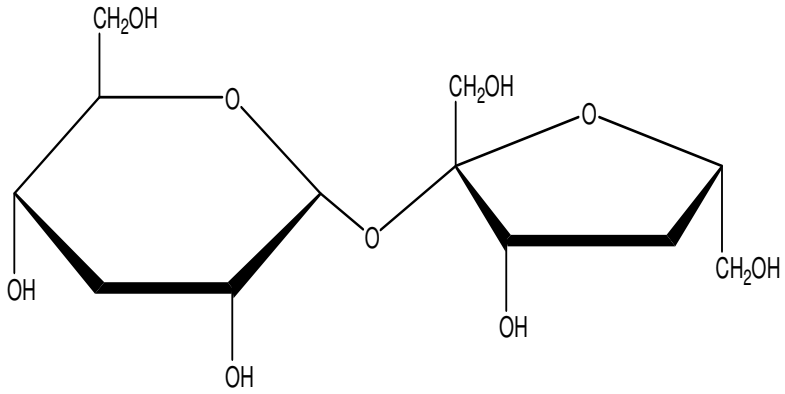
Synonym : Beet sugar; cane sugar; α-β glucopyranosyl- β-D-fructofuranoside; refined sugar; saccharose; sugar

Chemical name : β-D-fructofuranosyl- α-β glucopyranoside

Empirical formula : $C_{12}H_{22}O_{11}$

Molecular weight : 342.30

Structural formula :



Functional category : Base for medicated confectionery,
Granulating agent,
Sugar coating adjuvant,
Suspending agent,
Sweetening agent,
Tablet and capsule diluents,
Viscosity increasing agent.

Description : It is colourless crystals, crystalline powder, Odourless and sweet taste.

TYPICAL PROPERTIES

Density	:	1.56 g/cm^3 (Crystalline sucrose)
		1.56 g/cm^3 (Powdered sucrose)
Density (bulk)	:	0.93 g/cm (Crystalline sucrose)
		0.60 g/cm^3 (Crystalline sucrose)
Density (tapped)	:	1.03 g/cm^3 (Crystalline sucrose)
		0.82 g/cm^3 (Powdered sucrose)
Melting point	:	160 -186°C (with decomposition)
Solubility	:	Practically insoluble in Chloroform at 20°C
		Soluble in 1 in 0.5 parts of Water at 20°C

Incompatibilities : It may be contaminated with traces of heavy metals which can lead to in compatible with active ingredients.Eg Ascorbic acid.

It is also incompatible with aluminium.

Applications :

- It is widely used in oral pharmaceutical formulations.
- Sucrose syrup containing 50-67 % w/w sucrose.
- Binding agent wet granulation in the tableting.
- Large amount of sucrose may harden to give poor disintegration in the tablet manufacturing.

GLYCERIN[74]

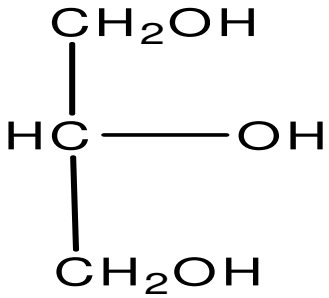
Synonym : Croderol; glycerine; glycon G-100; kemstrene; pricerine;1,2,3,-propanetriol; trihydroxy propane glycerol

Chemical name : Propane-1,2,3-triol

Emperical Formula : $C_3H_8O_3$

Molecular Weight : 92.09

Structural formula



Functional category : Antimicrobial preservative,
Emollient,
Humectant,
Plasticizer,
Solvent,
Sweetening agent,
Tonicity agent.

Description : Clear, colorless, odorless, viscous, hygroscopic liquid, it has a sweet taste, approximately 0.6 times as sweet as sucrose.

TYPICAL PROPERTIES

Boiling point : 290°C

Density : 1. 2656 g/cm^{3}at 15°C
1. 2636 g/cm^{3}at 20°C

		1. 2620 g/cm^{3}at 25°C
Melting point	:	17.8°C
Solubility	:	Slightly soluble in Acetone Practically insoluble in Benzene Miscible with Ethanol(95%) and Water
Incompatibilities	**:**	It may explode if mixed with strong oxidizing agents, such as chromium trioxide and potassium chlorate. Black discoloration of glycerine occurs in the presence of light on contact with zinc oxide.

Applications

- It is also used in cosmetics and as a food additive.
- It's used as a therapeutic agent in a variety of clinical applications.

PROPYL PARABEN[74]

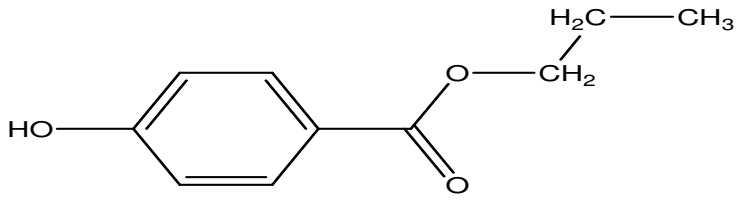
Synonym : 4 – hydroxyl benzoicacid propylester; propyl p-hydroxy benzoate; propyl para hydroxy benzoate; propyl paracept

Chemical Name : Propyl 4 –hydroxy benzoate

Empirical formula : $C_{10}H_{12}O_3$

Molecular Weight : 180.20

Structural formula



Functional Category : Antimicrobial preservative

TYPICAL PROPERTIES

Solubility : Freely soluble in Acetone and Ether at 25°C

Soluble in Water in 1 in 25 parts at 80°C

Description : White, crystalline, odourless and tasteless powder

Incompatibilities : The antimicrobial activity of propyl paraben considerably reduce in the presence of non ionic surfactants as a result of micellization. Absorption of propyl paraben by plastics has been reported. Propyl paraben is discoloured in the presence of iron.

Applications

- It is used as an antimicrobial preservative in cosmetic formulations.
- Propyl paraben (0.02%) together with methyl paraben (0.18 %) has been used for the preservation of varios parenteral pharmaceutical formulations.

TWEEN 80[74]

Synonym : Polyoxyethylene 20 oleate

Chemical name : Poly oxy ethylene 20 sorbitan oleate

Empirical formula : $C_{64}H_{124}O_{26}$

Molecular Weight : 1310

Functional category: Emulsifying agent,
Non-ionic surfactant,
Solubilizing agent,
Wetting agent.

Description : It have a characteristic odour, warm, bitter taste, yellow oily liquid form at 25°C

TYPICAL PROPERTIES

Moisture content : 3.0(%)

HLB value : 15.0

Viscosity : 425 mpas

Specific gravity : 1.08 at 25°C

Solubility : Soluble in Ethanol and Water
Insoluble in mineral oil and Vegetable oil

Incompatibilities : Discoloration and precipitation occurs with various Substances, especially phenols, tannins, tar-like materials. The antimicrobial activity of paraben preservatives is reduced in the presence of polysorbates.

Applications

- Hydrophilic non-ionic surfactants used widely as emulsifying agent in the preparation of stable oil in water pharmaceutical emulsion.
- It may also be used as solubilizing agents.

XANTHAN GUM[74]

Synonym : Corn sugar gum, poly saccharide

Chemical name : Xanthan gum

Empirical formula : It is a high molecular weight polysaccharide gum. It contains D-glucose, D- mannose as the dominant hexose units along with D- glucuronic acids.

Functional Category: Stabilizing agent, Suspending agent, Viscosity-increasing agent.

Description : Cream or white coloured, odourless, free flowing fine powder.

TYPICAL PROPERTIES

Activity / Alkalinity : pH – 6-8 for 1 % w/v aqueous solution

Melting Point : Chars at 270 °C

Solubility : Practically insoluble in ethanol and ether,

Soluble in cold and warm water.

Viscosity : 120-1600 cps for 1 % w/v aqueous Solution at 25°C

Incompatibilities : Xanthan gum is an anionic material is not usually Compatible with cationic surfactant. Polymersand preservatives since precipitation occur. It is compatible with most synthetic and natural viscosity increasing agents. It must be stable in the presence of 60% water miscible organic solvents.

Applications

- It is used in Oral and topical pharmaceutical formulations, cosmetics and food products.
- It is also used as a suspending and stabilizing agent

INDION -204 [75]

Matrix type : Derived from cross linked poly acrylic acid

Functional group : Carboxylic acid

Standard ionic form : H^+

SPECIFICATIONS PHYSICAL PROPERTIES

Particle size range : ≤0.15

% moisture : ≤ 5

Total exchange Capacity meq/g(dry) : 10.0

Solubility : Insoluble in water and common solvents.

Appearance : White to off white flowing powder.

Chemical properties : Polymeric functional group –carboxylic acid

Applications : Taste Masking Agent: A drug polymer adduct can be synthesized due to the ionic bond between the bitter and the polymer thus masking the objectionable bitter taste of the drug since the polymer drug adduct is formed. It is tasteless in the mouth, but it dissociates in the acidic pH of the stomach, the bio availability of the drug is not affected.

Toxicity : It is a high molecular weight polymer so can't be absorbed by body tissue and it is safe for human consumption. It has no any physiological action recommended dosage and it is non –toxic.

Storage : Stored in a tightly container, keep away from the moisture, moisture is absorbed drug at 900° c to 1000°C to remove moisture content below 10%

Packing : 5 kg, 20 kg in corrugated box.

Materials and methods

MATERIALS AND METHODS

Table 2:List of materials and their applications in formulation.

Name of the material	Manufacturer/ supplier	Use in formulation
Roxithromycin IP	Apex Laboratories P Ltd	Active Ingredient
Indion-204	Ion exchange (India) Ltd, Mumbai	Cation Exchange Resin
Sucrose	Cooperative sugar mills (Pvt) Ltd, Pondy	Sweetener
Sorbitol Solutions (70%)	Gayathri starch kem Ltd, Andra Pradesh	Sweetener
Xanthan gum	D.K.Enterprises(Archerdaniersmidland company), USA	Suspending Agent
Propylene glycol IP	Manali petro chemicals (Pvt) Ltd, Chennai	Solvent for preservative
Sodium Benzoate IP	Ganesh Benzo Plast, Uma Lakshmi and Co, Chennai	Preservative
Methyl paraben IP	Salicylates Chemicals, Hyderabad	Preservative
Propyl Paraben IP	Salicylates Chemicals, Hyderabad	Preservative
Citric Acid monohydrate	Solaris Bio Chemicals Ltd, Vadodra	Acidulant
Sodium Citrate IP	Sunil chemicals, Uma Lakshmi and Co, Thane Dist	Buffering agent
Sodium chloride	Southern fine kem India Ltd.,Chennai	Electrolyte
Glycerin	Godrej industries Ltd,Mumbai	Viscosity builder
Sunset Yellow FCF	Roha dye chem, Indiras agencies, Maharastra	Colouring agent
Tween-80	Laffans petro chemicals Ltd, Gujrat	Wetting agent
Masking Flavour 2521	Firmenich aromatics India (Pvt)Ltd, Daman	Flavouring agent
Orange oil Flavour	Firmenich aromatics India (Pvt)Ltd, Daman	Flavouring agent

Table 3: List of Instruments/Equipments used

S.No	Instruments/Equipments	Manufacture/ Supplier
1.	Electronic weighing balance	Shimadzu, Japan
2.	Brook Field Digital Viscometer	Brook Field, German
3.	pH Meter	Digisun Electronics, Hyderabad
4.	Dissolution Test Apparatus	Veego (VDA-60)
5.	UV- Visible Spectrophotometer	UV Pharma Spec1700, SHIMADZU
6.	Water bath	In Lab Equipments (Chennai) Pvt. Ltd
7.	Humidity chamber	In Lab Equipments (Chennai) Pvt. Ltd

The objective of the present work to be achieved in the following steps.

- Preformulation studies
- Complexation of drug with Resin
- Development of suspension
- Evaluation of suspension
- Stability studies

Preformulation studies [76]

Preformulation investigations are designed to deliver all necessary data (especially physicochemical and Biopharmaceutical properties of drug substance, excipients and packaging materials) which may influence

- Formulation design
- Method of manufacture of drug substance and drug product
- Pharmacokinetic/Biopharmaceutic properties of the resulting product
- Packaging of the product

Preformulation steps:

1. Calculation of many of the important physico-chemical characteristics of drug – Solubility.

PROCEDURE

Solubility of API and the excipients in different selected media was determined by dissolving the known quantity in cumulative manner with the aid of sonication till the API or the excipients remains insoluble in the media.

Preparation of 0.1N Hydrochloric Acid (1.2pH)

8.5ml of the hydrochloric acid was taken and dissolved in water and made upto 1000ml to get 0.1N hydrochloric acid.

DETERMINATION OF λ_{max} [77]

30g of Ammonium acetate was dissolved in 50 ml of water. 1 ml of Acetyl acetone was added and the final volume was adjusted to 100ml with water and stored in refrigerator. Freshly prepared reagent was used in the analysis. 250mg of Potassium permanganate was dissolved and diluted to 100 ml with water. 10gm of Oxalic acid was dissolved and diluted to 100ml with water. 250mg of Roxithromycin was accurately weighed and transferred to a 100ml volumetric flask. It was dissolved in 20ml of glacial acetic acid and diluted to 100ml with distilled water. 5ml 0f an aliquot was further diluted in 50ml of water to obtain the final concentration of 250 µg/ml.

In a 10ml volumetric flask, 2ml of standard Roxithromycin solution and 1ml glacial acetic acid solution were pipetted successively. 0.2ml of potassium permanganate solution was added. The reaction mixture was heated on water bath at 37°C for 10min. Excess of potassium permanganate was neutralized with oxalic acid. 2ml of reagent solution was added to it and mixed thoroughly. The reaction mixture was heated on water bath at 37°c for 1min and cooled. The volume was adjusted upto the mark with water. Absorbance of the coloured solution was scanned on UV-Visible spectrophotometer from 600nm to 200nm against reagent blank. Maximum absorbance was obtained at 412nm.

PREPARATION OF CALIBRATION CURVE

25mg of Roxithromycin was weighed accurately and transferred to a 100ml standard flask. To that 1ml of Hydrochloric acid was added and the volume was made upto the mark using deionized water. From the stock solution 2, 4, 6, 8 and 10ml was pipetted out in a 10ml standard flask. To each of the standard flask, 0.2ml of potassium permanganate solution was added. The mixture was heated on water bath for 10 min at 37 °C. Excess of potassium permanganate was neutralized with oxalic acid. 2ml of reagent solution was added to it and mixed thoroughly. The mixture was heated on water bath for 1 min at 37° C and cooled. The volume was adjusted upto the mark with deionized water. Absorbance of the solution was measured against a reagent blank at 412nm.

FORMULATION DEVELOPEMENT

Following ingredients were selected to develop the desired formulation.

Table 4: Formulation of suspension

S.No	Ingredients	S-1	S-2	S-3	S-4	S-5	S-6	S-7
1	Roxithromycin (g)	10	10	10	10	10	10	**10**
2	Indion-204 (g)	2.5	5	7.5	10	20	25	**30**
3	Sucrose (g)	300	300	300	300	300	300	**300**
4	Xanthan gum (g)	1.5	1.5	1.5	1.5	1.5	1.5	**1.5**
5	Tween 80 (g)	0.5	0.5	0.5	0.5	0.5	0.5	**0.5**
6	Sorbitol (g)	100	100	100	100	100	100	**100**
7	Propylene glycol (g)	50	50	50	50	50	50	**50**
8	Methyl paraben (g)	1	1	1	1	1	1	**1**
9	Propyl paraben (g)	0.5	0.5	0.5	0.5	0.5	0.5	**0.5**
10	Sodium citrate (g)	1.5	1.5	1.5	1.5	1.5	1.5	**1.5**
11	Citric acid (g)	1	1	1	1	1	1	**1**
12	Sodium chloride (mg)	1.25	1.25	1.25	1.25	1.25	1.25	**1.25**
13	Glycerin (g)	50	50	50	50	50	50	**50**
14	Mint flavour (ml)	10	10	10	10	10	10	**10**
15	Orange oil flavour (ml)	5	5	5	5	5	5	**5**
16	Sunset yellow FCF (mg)	25	50	50	50	50	50	**50**
17	DM Water	q.s	q.s	q.s	q.s	q.s	q.s	**q.s**

PROCEDURE [78]

Step -1

Drug and ion exchange resins were weighed accurately. Then the resin was poured into DM water. The drug was added in to the resinate with continuous stirring to get drug resinate.

Step -2

Sucrose was added to 150 ml of DM water and boiled for complete dissolving of sucrose. Then the sorbitol was mixed with the sugar solution.

Step -3

Xanthan gum was poured in to glycerin and mixed to dissolve the gum completely.

Step-4

Tween 80 was added in to the drug resinate. The sugar, sorbitol solution and xanthan gum solution were added in to the drug resinate formulation.

Step -5

Methyl paraben and propyl paraben were added separately into propylene glycol and dissolved completely. This was added to the drug resinate formulation.

Step-6

Sodium citrate, citric acid and sodium chloride were dissolved in DM water and poured in to the drug resinate formulation.

Step-7

The flavors and colour were added into the drug resinate formulation. Finally suspension was made up to 1000 ml with DM water and mixed for 30 minutes.

EVALUATION OF SUSPENSIONS

Taste evaluation of optimized formulation[79]

The taste evaluation was performed with 10 volunteers in the age group of 19-25 yrs. The Formulation (S-7) was held in the mouth for 15 seconds by each volunteer and the bitterness level was recorded against pure drug using a numerical scale.

pH

pH is be defined as the negative logarithm of hydrogen ion concentration.

Mathematically it is written as

$$\mathbf{pH = \log \ 1/ [H_3O^+]}$$

Since the logarithm of 1 is zero.

The equation may also be written

$$\mathbf{pH = - \log(H_3O^+)}$$

- **Determination of pH** [80]

pH of suspension was determined by using pH meter. pH of the phases of suspension also contributes to stability and characteristic of formulations. pH of the suspension was recorded from time to time.

Viscosity

Viscosity of suspension is a great importance for stability and palatability of suspensions. Suspensions have least physical stability amongst all dosage forms due to sedimentation and cake formation.[78]

Sedimentation is governed by stoke's law,

$$\mathbf{V = d^2 (\rho_s - \rho_l) \ g / 18 \ n}$$

V - terminal settling velocity

d –diameter of the settling particle

ρ_s – density of the settling solid (dispersed phase)

ρ_l - density of the liquid (dispersion medium)

g – Acceleration due to gravity

Ƞ – viscosity of dispersion medium

when the viscosity of dispersion medium increases the settling velocity decreases.

- **Determination of viscosity[81]**

The viscosity of suspension was determined at ambient condition using Brookfield digital viscometer taking adequate amount of the sample.

Sedimentation Volume [80]

Sedimentation volume F is the ratio of equilibrium volume of sediment (Vu) to the total volume of suspension (Vo).[77]

$$F = Vu / Vo$$

Vu - Volume of sediment

Vo - total volume of suspension

The sedimentation volume F normally ranges from less than 1 to 1. When F=1, the sediment volume and the total volume are equal and such a suspension is pharmaceutically acceptable.

- **Determination of sedimentation volume [80]**

Sedimentation volume was determined as a function of time. 50ml suspension was transferred to a 100 ml measuring cylinder of 2.5cm diameter. The sedimentation volume F was determined.

Assay[77, 79]

Accurately measured volume (5ml) of suspension was transferred to a 50ml volumetric flask, the volume was made up with 0.1N HCl to break the complex and sonicated for 30min. To the above solution 0.2ml of potassium permanganate was added and heated for 10 mins at 37°C. The excess of potassium permanganate was neutralized with oxalic acid. To the resulting mixture, 2ml of reagent solution was added and heated at 37°C for 1 min. The absorbance of the resulting solution was measured at 412nm taking a reagent blank.

***In vitro* Dissolution study** [77, 79]

Dissolution profile of Roxithromycin suspension was determined using the USP (type II) paddle apparatus with a speed of 50 rpm. Dissolution was tested in acidic buffer 0.1N HCl of 900ml at 37 ±0.5˚C. Aliquot volume was withdrawn at 10, 20, 30 and 60 min and filtered throught 0.45µ membrane filter. To that 0.2ml of potassium permanganate was added and heated for 10 min at 37°C. The excess of potassium permanganate was neutralized with oxalic acid. To the resulting mixture, 2ml of reagent solution was added and heated at 37°C for 1 min. The absorbance of the resulting solution was measured at 412nm taking a reagent blank.

MICROBIAL TESTING[82]

MICROBIAL TESTING OF FINISHED PRODUCT

This test is mainly performed to check whether the finished product has any presence of micro organism or not.

For this test two media were commonly employed namely,

1. Tryptone Soya Agar Medium (TSA) for bacteria.
2. Sabouraud's Chloramphenicol Agar Medium (SCA) for yeast and moulds.

STEPS[82]

1. TSA and SCA medium were prepared and autoclaved for 15 min at 121°C.
2. 10ml of the sample was added to the broth and mixed well.
3. By using a micropipette, 1 ml from the broth was transferred to two sterile petridishes, One for bacteria and the other for fungi.
4. 20 ml of the TSA and SCA medium was poured into their respective plates
5. The plates were then rotated in clockwise and anti-clockwise directions for even spreading of the sample.
6. The plates were allowed for solidification.
7. TSA plate was incubated at 37°C for 48 hours in an inverted position.
8. SCA plate was incubated at 20 -25°C for 5 days in an upright position.
9. The colonies formed were counted and recorded.

LIMITS[82]

Bacteria ***: not more than 300 colonies per plate.***

Fungi ***: not more than 100 colonies per plate.***

FORMULA (CFU/ML) = $\frac{\text{No.of colonies X Amount of Sample taken}}{\text{Dilution factor}}$

PATHOGEN TESTING[82]

This test is done only if the inoculated plate shows coloured colonies which indicates the presence of pathogens.

The pathogens are

Escherichia coli

Salmonella species

The following media were employed.

a) Bismuth sulphite agar

Selective for *Salmonella species* and produce black coloured colonies.

b) Eosin methylene blue agar:

Selective for *E.coli species* and produce green coloured colonies with metallic sheen.

STABILITY TESTING [83, 84]

STABILITY STUDIES OF THE FINISHED PRODUCT

Stability of a drug can be defined as the time from date of manufacture and packaging of the formulation until its chemical or biological activity is not less than a predetermined level of labeled potency and its physical characteristics have not changed appreciably or deleteriously. Although there are exceptions, 90% of labeled potency is recognized as the minimum acceptable potency level.[83]

The international conference on Harmonization (ICH) Guideline titled "stability testing of new drug substance and products" (QIA) describes the stability test requirements for drug registration application in the European Union, Japan and USA.[84]

ICH specifies the length of study and storage conditions.

- Long term testing 25°C ± 2°C /60 % RH ± 5% for 12 months
- Accelerated testing 40°C ± 2°C/75% RH ±5% for 6 months
- Refrigerated conditions 5°C ± 3°C. for 3 months

Stability studies for the present work was carried out at 25°C ± 2°C / 60% RH and 40°C ± 2°C / 75 % RH for the selected formulation for three months and at 5°C ± 3°C refrigerated conditions for 3 months.

METHOD

The selected formulations were packed in wide mouth bottle. They were stored at 25°± 2°C /60%± 5% RH and 40° ± 2°C /75%± 5% RH for 3 months in humidity chamber and evaluated for their physical appearance and drug content at specified intervals of time.

Results and discussion

RESULTS AND DISCUSSION

PREFORMULATION STUDIES

Solubility Studies

Solubility studies were done for candidate drug and excipients as per requirement of development.[74]

Table 5: Solubility of ingredients in different solvent

Solute	Ethanol	Ether	Water	Acetone	Chloroform
API	Freely soluble	ND	In soluble	Freely soluble	ND
Sucrose	ND	ND	Very soluble	ND	In soluble
Xanthan gum	In soluble	In soluble	soluble	ND	ND
Tween80	Soluble	In soluble	soluble	ND	ND
Sorbitol	Slightly soluble	In soluble	Very soluble	ND	In soluble
Sodium citrate	In soluble	ND	Freely Soluble	ND	ND
Citricacid monohydrate	Freely Soluble	Sparingly soluble	Very soluble	ND	ND
Sodium chloride	Slightly soluble	ND	Freely Soluble	ND	ND
Sodium benzoate	Sparingly soluble	ND	Freely Soluble	ND	ND
Glycerin	Miscible	ND	Miscible	Slightly soluble	In soluble
Propylene glycol	Miscible	Soluble	Miscible	Miscible	Miscible
Methyl paraben	Freely Soluble	ND	Slightly soluble	ND	ND
Propyl paraben	Freely Soluble	Freely Soluble	Slightly soluble	ND	ND

*** ND – Not Dissolved**

Roxithromycin was soluble in ethanol and insoluble in water. All the ingredients were soluble in water.

CALIBRATION CURVE FOR ROXITHROMYCIN

Table 6: Data for Calibration Curve of Roxithromycin in 0.1N HCl

Concentration (mcg/mL)	Absorbance
0	0.0000
2	0.1600
4	0.3300
6	0.4970
8	0.6570
10	0.8310

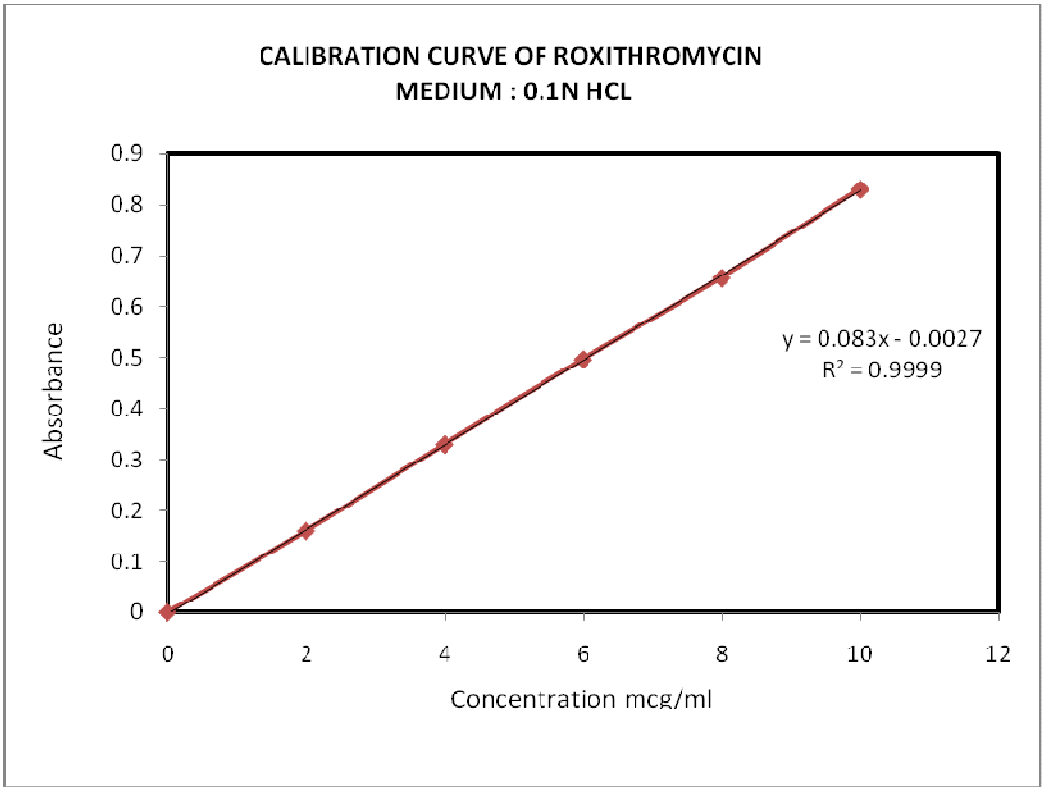


Fig.1: Calibration Curve of Roxithromycin

It was found that the solutions of Roxithromycin in 0.1N Hcl show linearity (R^2= 0.999) in absorbance at concentrations of 2-10mcg/ml and obeys Beer Lambert Law.

FORMULATION DEVELOPMENT

(a) Evaluation of Formulated Roxithromycin Suspension

Table 7:Evaluation of Roxithromycin suspension

S.No	Test for evaluation	Observation						
		S -1	**S - 2**	**S- 3**	**S- 4**	**S -5**	**S – 6**	**S - 7**
1	Taste	Bitter	Bitter	Bitter	Bitter	Bitter	Slightly Bitter	Not Bitter
2	pH	3.54	3.58	3.61	3.67	3.70	3.64	3.66
3	Viscosity (Cps)	576	589	632	648	644	652	665
4	Sedimentation volume (F)	0.94	0.95	0.96	0.97	0.97	0.99	0.99

Inference

- Oral suspensions were formulated in different combinations S-1, S-2, S-3, S-4, S-5,S-6,S-7
- From the above formulations, it was found that the bitter taste was not masked for formulations S-1, S-2, S-3, S-4 & S-5.
- Slightly bitter taste was observed in the formulation, S-6.
- The taste was completely masked in formulation S-7.
- The pH of formulations S-1 to S-7 ranged from 3.54 to 3.70 and the viscosity ranged from 576 to 665 Cps.
- The sedimentation volume (F) ranged from 0.94 to 0.99.

ASSAY

The drug content of the formulated suspension are given in table 8

Table 8: Assay of formulated Roxithromycin suspension

S.No	Formulation	Drug content (%)*
1	S -1	98.9 ± 0.0031
2	S -2	97.85 ± 0.1021
3	S -3	99.70 ± 0.187
4	S -4	98.34 ± 0.1542
5	S -5	99.16 ± 0.0021
6	S -6	99.89 ± 0.078
7	S -7	99.78 ± 0.0245

***Mean ±SD (n=3)**

INFERENCE

The drug content of the suspension ranged from 97.85% to 99.85%.The drug content of the formulation were within the limits.[79]

Table 9: *In vitro* drug release of formulated Roxithromycin suspension

Time (min)	CUMULATIVE % DRUG RELEASE*						
	S-1	**S-2**	**S-3**	**S-4**	**S-5**	**S-6**	**S-7**
10	79.44 ± 0.02	74.62± 0.0500	72.05± 0.0360	69.05± 0.0150	67.02± 0.0458	65.44± 0.0321	59.82± 0.0568
20	95.81± 0.0057	91.86± 0.0206	83.43± 0.0264	80.89± 0.0046	80.12± 0.0251	78-47± 0.0300	75.02± 0.0512
30	99.79± 0.0100	99.88± 0.0152	97.92± 0.0125	93.25± 0.0600	92.22± 0.0642	86.19± 0.0808	84.02± 0.0611
60	-	-	99.82± 0.0264	99.72± 0.0400	99.72± 0.0305	99.86± 0.0360	99.62± 0.0850

***Mean ±SD (n=3)**

INFERENCE

As the concentration of the resin was increased, the release of the drug from the formulation was sustained. Formulation S-1 & S-2 showed maximum release within 30 min.

IN VITRO RELEASE STUDIES

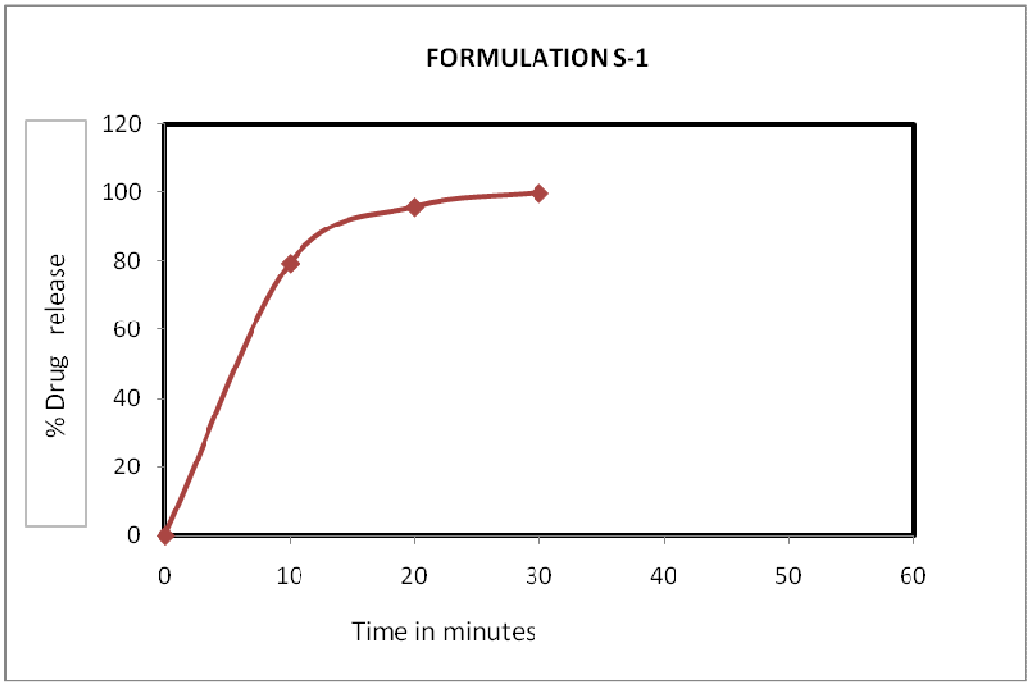


Fig. 2: *IN VITRO* RELEASE PROFILE S-1

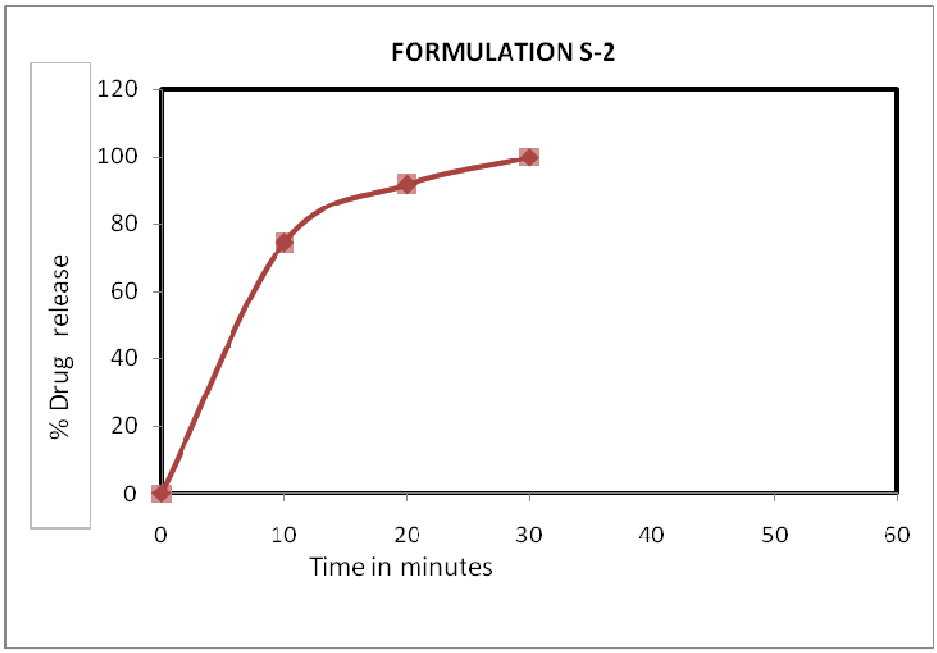


Fig. 3: *IN VITRO* RELEASE PROFILE OF S-2

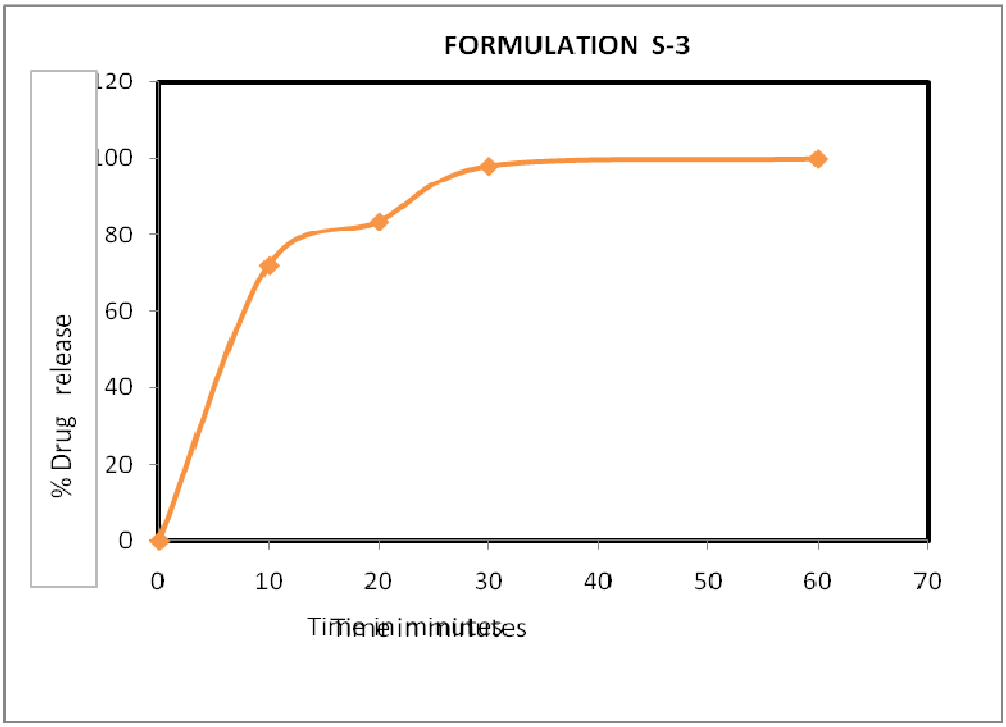


Fig. 4: *IN VITRO* RELEASE PROFILE OF S-3

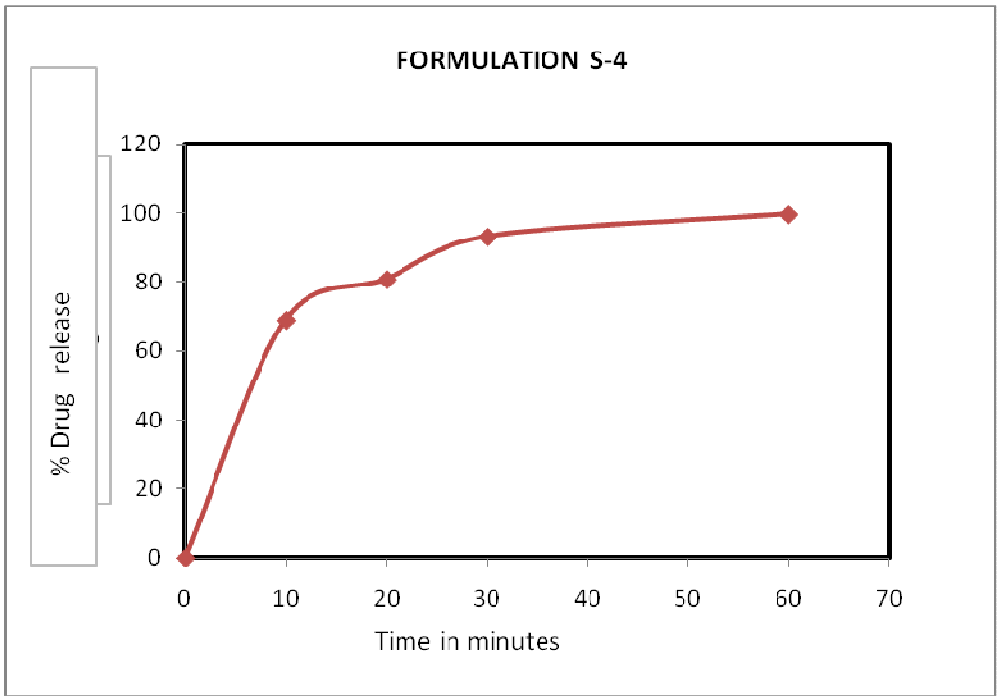


Fig. 5: *IN VITRO* RELEASE PROFILE OF S-4

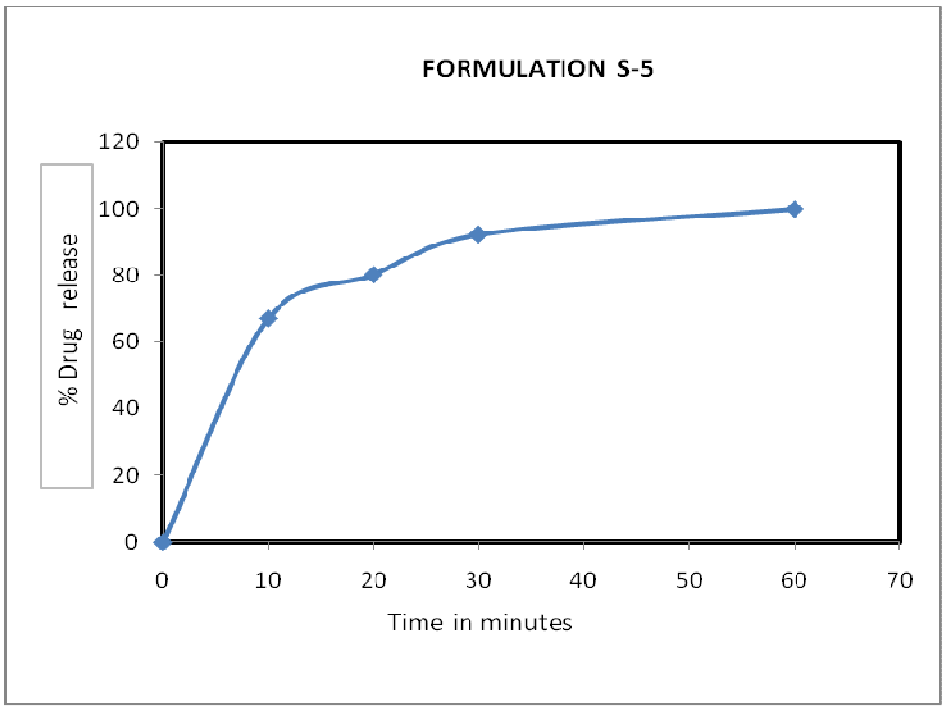


Fig. 6: *IN VITRO* RELEASE PROFILE OF S-5

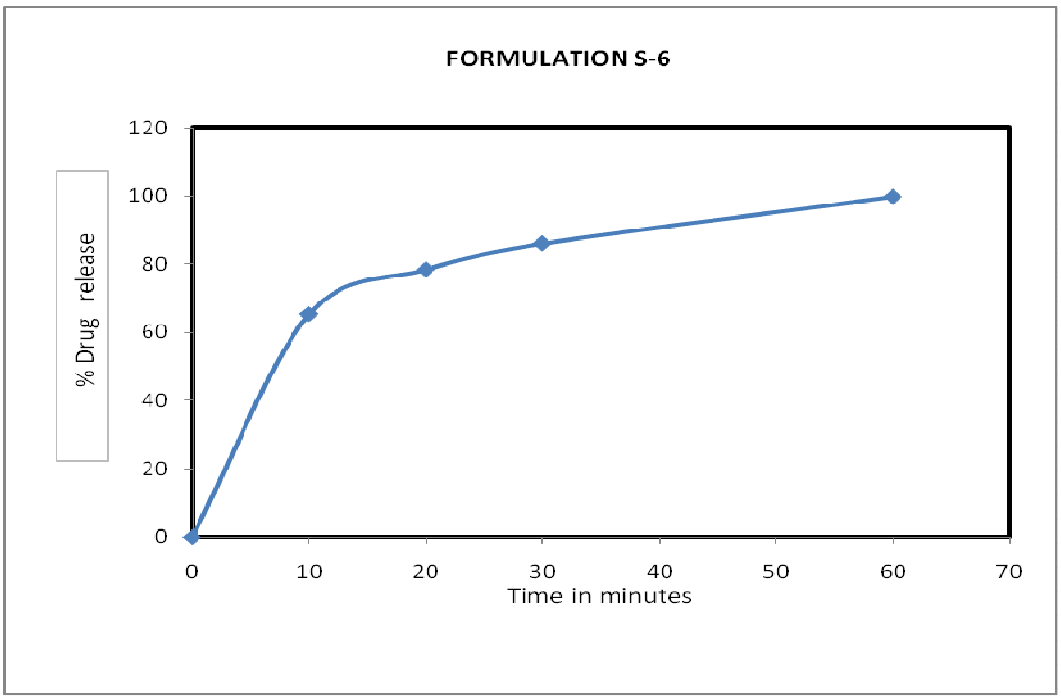


***Fig. 7: IN VITRO* RELEASE PROFILE OF S-6**

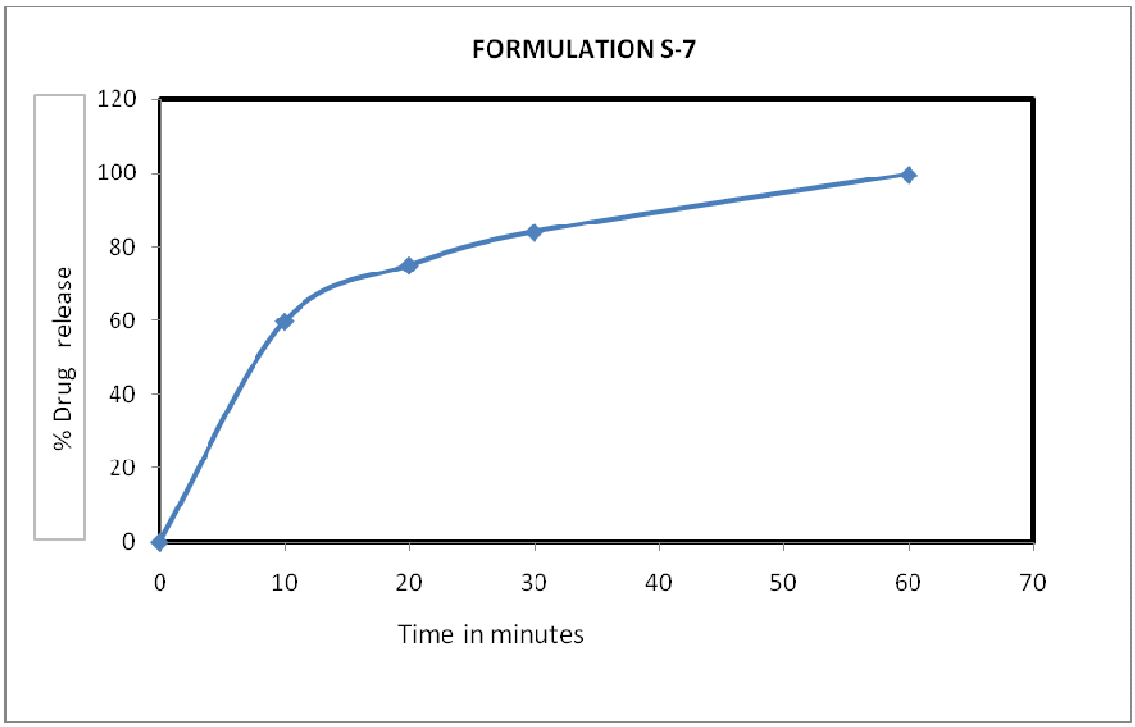


***Fig. 8: IN-VITRO* RELEASE PROFILE OF S-7**

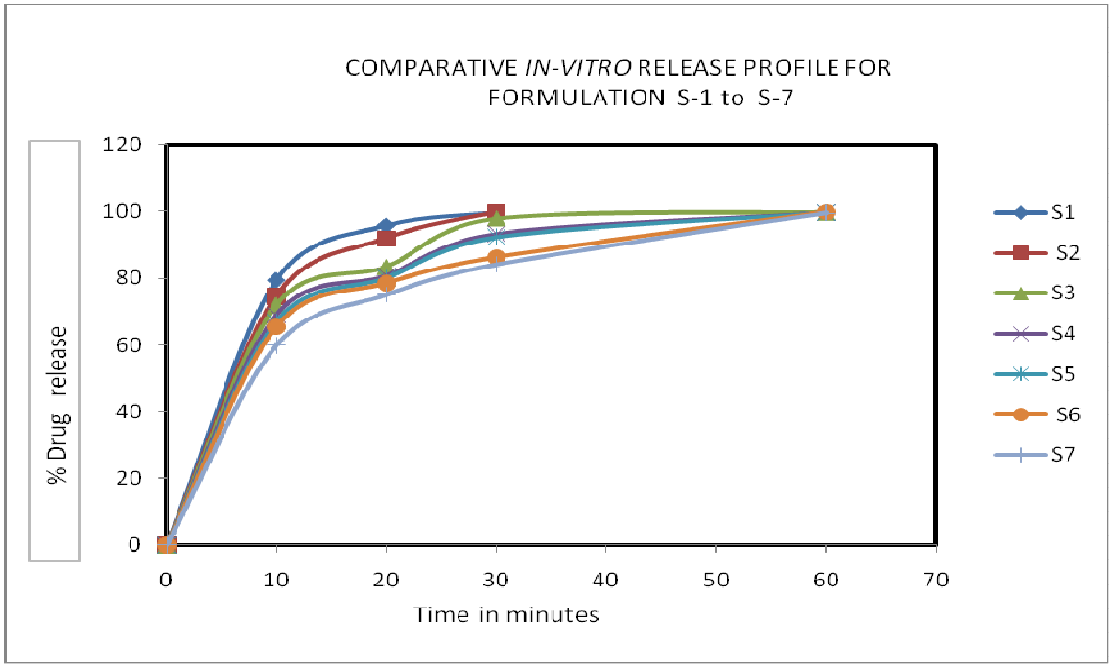


Fig. 9: COMPARATIVE *IN-VITRO* RELEASE PROFILE OF S-1 to S-7

Table-10: COMPARATIVE EVALUATION OF MARKETED SAMPLE AND FORMULATION S-7

S.No	Test for evaluation	Observation	
		Marketed sample	**Formulation S –7**
1	Taste	Slight Bitterness observed	Bitterness completely masked
2	pH	3.68	3.66
3	Viscosity (Cps)	660	665
4	Sedimentation volume (F)	0.99	0.99
5	Colour	Orange	Pale yellow
6	Drug Content * (%)	99.03 ±0.0267%	99.78 ±0.0245%

***Mean ±SD (n=3)**

INFERENCE

From the comparative study between marketed sample and S7 formulation it was found that the bitter taste of Roxithromycin was completely masked in formulations S7. The other parameters were found to be the same as with marketed formulation.

Table11: COMPARATIVE DISSOLUTION PROFILE OF OPTIMIZED FORMULATION S-7 WITH MARKETED SAMPLE

Time (min)	% DRUG RELEASED*	
	Marketed sample	Formulation S-7
10	61.98±0.0929	59.82±0.0568
20	75.35±0.0513	75.02±0.0512
30	83.98±0.0953	84.02±0.0611
60	99.79±0.0624	99.62±0.0850

***Mean ±SD (n=3)**

The *in vitro* drug release from the marketed sample and formulation S-7 are similar.

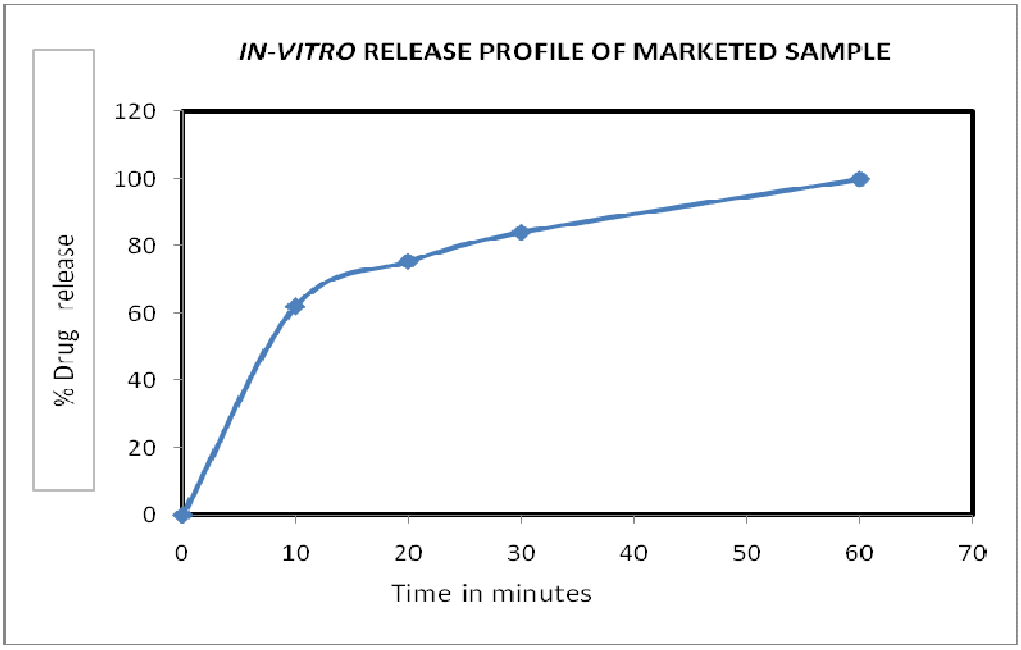


Fig.10: *IN VITRO* RELEASE PROFILE OF MARKETED SAMPLE

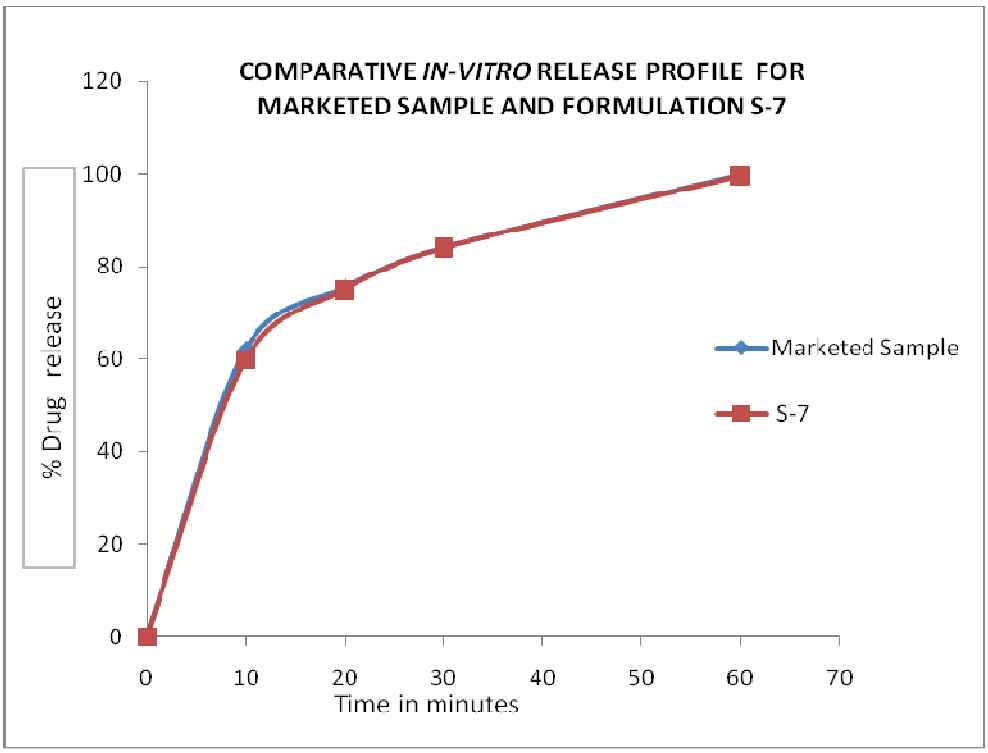


Fig.11: COMPARATIVE *IN VITRO* RELEASE PROFILE FOR MARKETED SAMPLE AND FORMULATION S-7

MICROBIAL TESTING

Table12: COLONY COUNTING (STABILITY CONDITIONS)

S.No	Observation	Accelerated condition (40±2°C/75±5%RH) for 3 months	Real time condition (25±2°C/60±5% RH) for 3 months	Refrigeration condition (5±3°C)for 3 months
1	BEFORE INCUBATION a) Total bacterial count	Nil	Nil	Nil
	b)Total fungal count	Nil	Nil	Nil
2	AFTER INCUBATION a) Total bacterial count	10 CFU/ml	Nil	Nil
	b)Total fungal count	Nil	Nil	Nil

Table 13: PATHOGEN TESTING (STABILITY CONDITIONS)

S.No	Pathogens	Accelerated condition (40±2°C / 75±5% RH) for 3 months	Real time condition (25±2°C/60±5% RH) for 3 months	Refrigeration condition (5±3°C) for 3 months
1	*Escherichia coli*	Absent	Absent	Absent
2	*Salmonella species*	Absent	Absent	Absent

INFERENCE

The best formulation (S7) was kept in different storage conditions. During the storage period the product was checked for microbial contamination. For this formulation (S7) there was absence of *pathogens*, 10 bacterial colonies are formed in the accelerated conditions, but it was found to be within the limits.[82] And there was no countable fungal colonies observed in the both accelerated and real time conditions.

STABILITY TESTING

Table 14: Stability Studies of formulated Roxithromycin Suspension (Formulation S-7)

S.No	Test for evaluation	Accelerated condition (40±2°C / 75±5% RH) for 3 months	Real time condition (25 ±2°C/ 60±5% RH) for 3 months
1	Taste	No change	No change
2	Colour	No change	No change
3	pH	3.74	3.67
4	Viscosity (Cps)	660	665
5	Sedimentation volume (F)	0.99	0.99
6	Drug content(%)*	98.06±0.0236	98.97±0.0423

***Mean ±SD (n=3)**

Table 15: Stability studies of formulated Roxithromycin Suspension under Refrigeration condition (Formulation S-7)

S.No	Test for evaluation	Refrigeration condition (5°C ± 3°C for 3months)
1	Taste	No change
2	Colour	No change
3	Ph	3.74
4	Viscosity (Cps)	660
5	Sedimentation volume(F)	0.99
6	Drug content (%)	98.06±0.0123
7	Appearance	Suspension is homogenous free from formation of crystals

***Mean ±SD (n=3)**

Table-16: *In vitro* drug release of Roxithromycin suspension

Time (min)	% DRUG RELEASED*		
	Accelerated condition (40 ±2°C/ 75±5% RH) for 3 months	**Real time condition (25±2°C/ 60±5% RH) for 3 months**	**Refrigeration condition (5±3°C) for 3 months**
10	58.02±0.002	59.85±0.0231	57.25±0.0265
20	70.56±0.0261	73.96±0.001	72.850±0.013
30	88.91±0.0354	81.86±0.0365	82.35±0.0355
60	97.08±0.0756	99.02±0.0023	98.65±0.0054

***Mean ±SD (n=3)**

INFERENCE

Stability studies of S-7 were carried out by placing the samples at different temperature and relative humidity (40 ±2°C/ 75±5% RH, 25±2°C/ 60±5% RH, 5±3°C) for 3 months in humidity chamber and evaluated. There is no significant change in release characteristics and other evaluation parameters. Based on the results it can be concluded that the formulated oral suspension was stable at room temperature over a period of 3 months. Even though stability is assured for 3 months, further studies at different temperature and humidity conditions are needed to establish its shelf life.

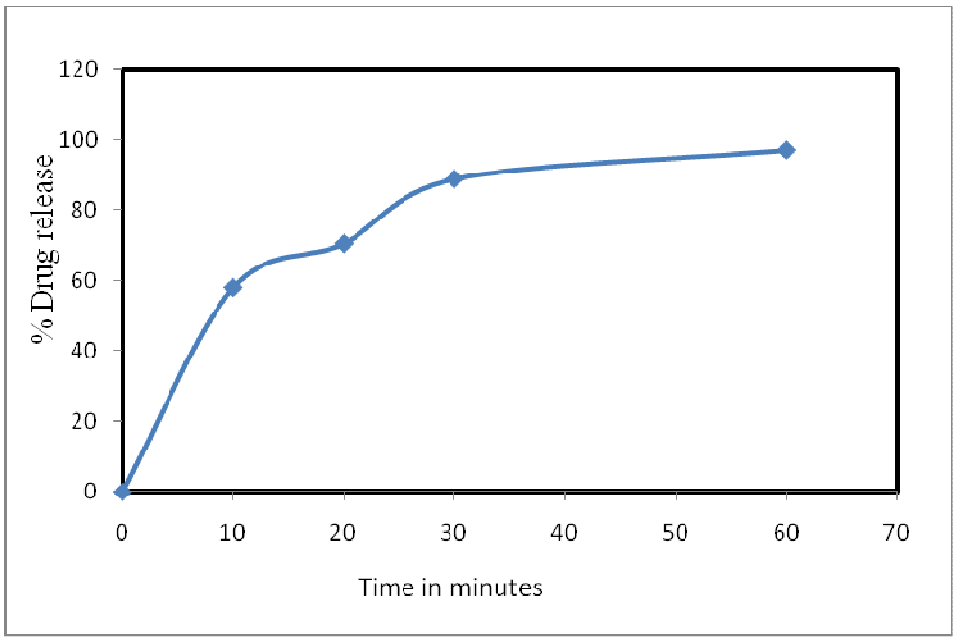


Fig.12: *In vitro* Release Profile for accelerated condition of optimized Roxithromycin Suspension

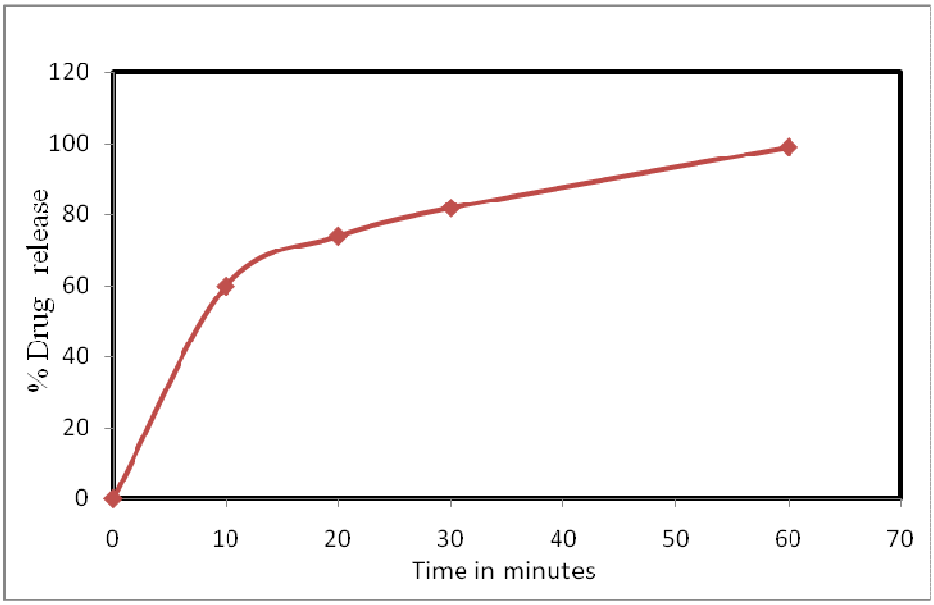


Fig-13:*In vitro* Release Profile for Real Time Condition of Optimized S7 Roxithromycin Suspension

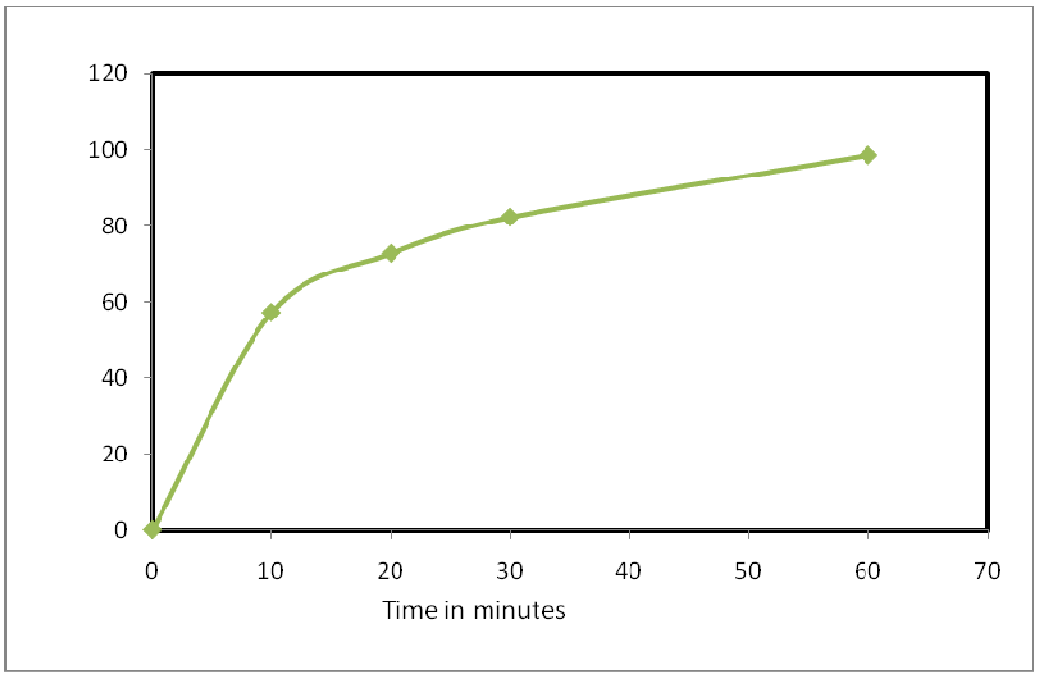


Fig.14: In vitro **Release Profile for Refrigerated Condition of Optimized S7 Roxithromycin Suspension**

Summary and conclusion

SUMMARY AND CONCLUSION

Several formulations were carried out by Drug-resin complexation method.

- It was concluded that the formulation S-7 was satisfactory than other formulations of S-1, S-2, S-3, S-4, S-5 & S-6.
- The formulations S-7 was compared with a leading brand of marketed sample and it was found to match with formulations S-7 in all aspects.
- The bitter taste was masked in formulations S-7 better than the marketed sample.

FUTURE WORK

- Scale up studies of the optimized formulation.
- To send the desired formulated lots for Bioequivalence studies.
- To proceed for exhibit batches.

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