altered liver function. However, gradual increase in the levels of serum total bilirubin, globulin, and serum enzymes noticed even in the drug administered groups from first to fourth week of treatment. These animals received CCl_4 biweekly for four weeks. Though the levels of these marker enzymes were slightly more than the control, they were significantly lower when compared to CCl_4 treated groups.

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Patient Compliant Dosage Form for Roxithromycin

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Roxithromycin, a macrolide antibiotic, is extremely bitter in taste. The present study deals with various techniques utilized for taste masking of roxithromycin viz granulation with Eudragit E 100 and complexation with ion exchange resins. Of these, complexation with ion exchange resins yielded complete taste masking. The drug resin complexation procedure was optimized with respect to parameters like taste of the resinate, drug to resin ratio and volume of medium. The complexation between roxithromycin and ion exchange resin was confirmed by differential scanning calorimetry. The taste-masked complex was then formulated into palatable mouth-dissolve tablets. The tablets were evaluated for various quality control parameters. Taste evaluation of the

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tablets showed complete masking of the bitterness of the drug. *In vitro* release studies revealed complete drug elution from the complex after a period of 30 min in pH 1.2 buffer.

Roxithromycin, chemically erythromycin 9 [o-(2-methoxy-ethoxy)-methyl-1]–oxime is a macrolide antibiotic. It is widely used in the treatment of mild to moderate infections of the ear, nose and respiratory tract[1,2]. Formulation of palatable solid dosage forms especially for pediatric and geriatric patients becomes a necessity[3,4]. Mouth dissolve tablets are dosage forms, which when placed in the mouth disintegrate or dissolve in the saliva within a minute without the aid of water or chewing. The faster the tablet dissolves, the quicker the absorption and ultimate onset of therapeutic effect. Mouth dissolve tablets are preferred to conventional dosage forms due to improved palatability. The rapidly disintegrating nature of mouth dissolve tablets and the convenience associated with its use offer dramatic improvement in patient compliance[5-7]. Thus, the objective of the present investigation was to mask the bitter taste of roxithromycin using various techniques and formulate it into a palatable mouth dissolve tablet that disintegrated in less than a minute.

One of the methods for taste masking of roxithromycin was using Eudragit, an acrylic resin, cationic in character, based on dimethylaminoethyl methaacrylate and neutral methacrylic acid esters. The other method for taste masking was use of ion exchange resins. Ion exchange resins are water insoluble, cross-linked polymers containing salt forming groups in repeating positions on the polymer chains. They are used in many industries including pharmaceutical industry for sustaining the release of the drug[8], to stabilize sensitive compounds[9], for taste masking[10] and as tablet disintegrants[11]. The ion exchange resin complexes with the drug through weak ionic bonding. Drug release from the resin depends on pH and electrolyte concentration within the gastrointestinal tract[12]. Indion 214 and Indion 204 are non-toxic and safe for human consumption. Indion 214 and Indion 204 have LD_{50} value of 10 000 mg/kg body weight and 4,500 mg/kg body weight, respectively by oral route.

Eudragit E 100 (methacryclic copolymer) was obtained as a gift sample from Colorcon Asia Pvt. Ltd., Mumbai. Indion 214 and Indion 204, which are cation exchange resins with cross-linked acrylic co-polymer matrix and having free carboxylic acid active group in hydrogen form were obtained as gift sample from Ion Exchange India Ltd, Mumbai. Roxithromycin was obtained from Alkem Laboratories Ltd., Mumbai. All solvents and reagents used were of analytical grade.

Taste masking of roxithromycin was attempted using Eudragit E 100. Roxithromycin was granulated with Eudragit E 100 solution in isopropyl alcohol (IPA) (10 %). The wet mass was screened through 16 mesh and dried in an oven for 45 min to 1 h at 60°. These dried granules were screened through a 40 mesh. Excipients such as diluents, superdisintegrants and sweeteners were granulated using PVP K29/32 as a binder. The blend was then compressed on Cadmach single stroke punch machine using 11 mm standard concave punches to give tablet weight of 300 mg. Various formulations were tried as shown in Table 1.

Taste masked complexes of roxithromycin were prepared by magnetic stirring method using double distilled water as the medium. Drug and resin were mixed in various ratios 1:1 to 1:5 on weight basis and stirred on a magnetic stirrer for a period of 4–8 h using different volumes of double distilled water as the medium. Non-bitter complex was yielded at 1:5 drug to resin ratio using 1000 ml of double distilled water when stirred for 6-8 h. The complex was vacuum filtered and then dried at 40º for an hour. To confirm complexation between roxithromycin and Indion 204, thermal behavior of roxithromycin and Indion 204 complex was recorded by differential scanning calorimetry (DSC).

The thermal behavior of roxithromycin was examined by DSC using Mettler Toledo Star System model. Approximately 10.0 mg of roxithromycin was loaded into an aluminium pan, hermetically sealed under nitrogen and run at a scanning rate of 10°/min over a temperature range of 40° to 240° in a dynamic nitrogen atmosphere. An empty sealed aluminium pan was used as reference. DSC thermogram of roxithromycin showed one endothermic peak of fusion, having a peak maximum of 121.2°. It showed a single, sharp, melting endotherm with an onset temperature of 117.3°.

Similarly, the thermal behavior of Indion 204 was recorded using DSC. Approximately 10.0 mg of Indion 204 was run at a scanning rate of 10°/min over a temperature range of 40° to 240°. DSC thermogram of the resin showed one endotherm of fusion, having a peak maximum of 120°. The thermal behavior of roxithromycin and Indion 204 (taste masked complex) was examined by running approximately 10.0 mg of the complex at a scanning rate of 10° /min over a temperature range of 40° to 240°. DSC curve of the complex showed one endothermic peak of fusion, having a peak

TABLE 1: FORMULATION OF ROXITHROMYCIN MOUTH-DISSOLVE TABLETS CONTAINING EUDRAGIT E 100

Ingredients (mg)	F1	F2	F3
Roxithromycin	50	50	50
Eudragit E-100 solution in IPA (10%)	6	8	8
Aspartame	15	15	15
Monoammonium Glycerrhizinate	10	10	10
Sodium saccharin	5	10	10
Sodium starch glycolate	8	8	8
Crospovidone	4	4	4
Croscarmellose sodium	10	10	12
Avicel PH101	106	99	97
Mannitol	50	50	50
Polyvinyl pyrrolidone K 29/32	15	15	15
Mixed fruit flavor	6	6	6
Peppermint flavor	3	3	3
Talc	6	6	6
Magnesium stearate	3	3	3
Aerosil	3	3	3

F1, F2 and F3 are different formulations tried with various concentrations of Eudragit E-100, Sodium saccharin and Croscarmellose sodium

maximum of 91.5°.

The taste-masked resinate was granulated along with diluent using PVP K29/32 as a binder. The wet mass was screened through 16 mesh and dried at 60° for 30 min. The dried granules were then screened through 40 mesh. Excipients were screened through 60 mesh. The blend was then compressed on Cadmach single stroke punch machine using 13 mm standard concave punches to give tablet weight of 500 mg. Various formulations were tried to achieve a palatable formulation. Formulations are as shown in Table 2.

The tablets were evaluated for various quality control parameters like appearance, taste, mouth feel, hardness, weight variation, *in vitro* dispersion time, *in vivo* disintegration time, drug content and drug release. Hardness of the tablets was determined with a Monsanto hardness tester. Taste of the tablets was evaluated by a panel of 10 healthy human volunteers. One tablet was placed in a beaker containing 6 ml of water. The time required for uniform dispersion of tablet was noted. *In vivo* disintegration time was determined by placing the tablet in the mouth. Drug content of the tablet was estimated by eluting the drug in 0.1 N methanolic HCl, filtering and recording drug content using colorimetry at 485 nm. *In vitro* drug release was determined using USP dissolution rate test apparatus II i.e. paddle type, in 500 ml of pH 1.2 buffer (0.1 N HCl) at a speed of 100 rpm. Aliquots were withdrawn at regular time intervals and estimated by colorimetry at 485 nm.

Complete taste masking of roxithromycin was not achieved with Eudragit E 100. The tablets also failed to disintegrate within a minute, thus the objective was not met with. The various formulations were compared with respect to *in vitro* dispersion time and taste. F1 had a bitter taste and failed to disintegrate completely leaving a hard core. Although F2 and F3 were well tolerated, both the formulations failed to comply with the requirement of disintegration test of mouth dissolve tablets (*in vitro* dispersion time of 80

TABLE 2: FORMULATION OF ROXITHROMYCIN MOUTH-DISSOLVE TABLETS CONTAINING INDION 204

Ingredients (mg)	F4	F5	F6
Roxithromycin Indion 204 complex	330	330	330
Aspartame	8	8	12
Monoammonium Glycerrhizinate	8	8	8
Sodium saccharin	5	5	5
Sodium starch glycolate	10	10	10
Croscarmellose sodium	8	10	10
Avicel PH101	86	84	80
Polyvinyl pyrrolidone K 29/32	25	25	25
Mixed fruit flavor	6	6	6
Menthol	2	2	2
Talc	6	6	6
Magnesium stearate	3	3	3
Aerosil	3	3	3

F4, F5 and F6 are different formulations tried with various concentrations of Aspartame and Croscarmellose sodium

s). Roxithromycin could be successfully taste masked with Indion 204. The process for preparing drug resinates was optimized with respect to parameters like drug to resin ratio, volume of the medium and taste of the complex. 1:5 ratio of roxithromycin and Indion 204 gave a completely taste masked complex which could be easily incorporated into mouth-dissolve tablets. Thus, disappearance of the Indion 204 peak as well as the drug peak in the DSC thermograms confirmed complexation between roxithromycin and Indion 204.

Hardness of formulations F4, F5 and F6 was found to be within the range 3-4 kg/sq-cm. The drug content of the formulations was within the range 98-110% of the labeled claim. F4 and F5 exhibited *in vitro* dispersion time of 45 s. F6 was found to be palatable with *in vitro* dispersion time of 30 s. Dissolution studies of F6 showed more than 80% release of the drug within 30 min. *In vitro* dispersion time as well as *in vivo* disintegration time of F6 was found to be 30 s indicating effective disintegration. All the volunteers found the tablets to be non-bitter.

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Differentiation in Hypocotyl Cultures of *Solanum platanifolium* Sims and Solasodine Production

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Hypocotyl cultures were developed from explants obtained from *in vitro* germinated seedlings of *Solanum platanifolium* Sims (Family-Solanaceae) on modified Murashige and Skoog's agar-solidified medium supplemented with 6-benzylaminopurine (2 ppm) and α-napthaleneacetic acid (1 ppm). Shoots originated from callus were transferred to modified Murashige and Skoog's medium and modified White's medium supplemented with different growth adjuvants. 6-benzylaminopurine (4 ppm) produced optimum growth of somatic shoots on MS medium. Chemical analysis of different tissues grown showed that organogenesis enhanced solasodine production.

Solanum platanifolium Sims is a good source of solasodine (1.93% dry weight)[1], a steroidal alkaloid that is easily converted into 16-dehydropregnenolone acetate, helpful in the synthesis of steroidal drugs employed for the treatment of sex harmone imbalances, oral contraceptives, asthma and inflammatory disorders. Plant tissue culture work on this plant is already in progress. Morphological differentiation in plant tissue cultures may affect the production of secondary metabolites e.g. alkaloid accumulation in callus of *S. dulcamara* was enhanced by the induction of organogenesis[2]. The aim of the present investigation

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