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● *RESEARCH NOTE* ●

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Optimization of different marketed grades of polymers for mucoadhesive suspension

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The oral route of drug administration is the most important method for administering drugs for systemic effects. When a new drug is discovered, one of the first questions, a pharmaceutical company asks is whether or not the drug can be effectively administered by the oral route, for its intended effect. From a patient's perspective swallowing a dosage form is comfortable and familiar means of taking medication. As a result, patient compliance and hence drug treatment is typically more effective with orally administered medications as compared to the non-conventional routes of administration (Dhirendra *et al.,* 2009). The development of oral dosage forms for poorly water soluble drugs and their bioavailability enhancement has been a challenge to formulation scientists in drug development. The three major factors that govern the rate and extent of bioabsorption from the GIT for such drugs are the permeability of drug to GI mucosa, their degree of solubility and retention time at absorption window. The inability to restrain and localize the system at gastrointestinal tract is one of the significant factors for low bioavailability of brick dust molecules formulated in the form of suspensions (Khan, 2001). In order to circumvent this problem, it has been proposed, successfully for several of them, to associate drugs to mucoadhesive polymeric systems because of their propensity to interact with the mucosal surface (Ponchel *et al*., 1998). This is finally requires not only for the local targeting of drugs but also for a better control of systemic delivery (Ahmed, Bonner and Desai, 2002). Currently however it is rather difficult to place the oral suspecsions at selective sites in the gastrointestinal tract for the long time, for this reason there have been considerable attempts to lower the fraction undergoing directly fecal elimination by increasing the bioadhesives interaction of the particles at the surface of intestinal membrane (Ben *et al.,* 1994; 1996).

Therefore the potential of a drug delivery system to localize a drug at the site of absorption for longer time and to promote intimate contact between the formulation and underlying absorption tissue has great appeal for both local and systemic effects. The idea of using bioadhesive polymers to prolong the contact time in the mucosal route of drug delivery was introduced in early 1980s, and since then it has attracted considerable attention from pharmaceutical scientists (Bernkop-Schnurch, 2005). This is a simple and yet highly innovative concept. Soon after the idea of mucoadhesion was introduced, its utility to pharmaceutical systems was studied (Park and Robinson, 1984) and since then large number of investigators have been involved in exploring the fundamental aspects of mucoadhesion and potential application of mucoadhesive dosage forms. In this context, the present study undertaken and designed to determine the rationale grade of Carbopol, a proven mucoadhesive polymer, for the formulation of mucoadhesive suspension dosage forms intended to improve bioavailability of poorly soluble drug - norfloxacin, patient compliance, reduce dose of drug and cost of formulation products.

Carbopol is acrylic acid polymer, carboxy-vinyl polymer, aldo known as polyacrylic acid available in the market in different grades *viz.,* carbomer 934P, 971P, 71G, 974P, resin share the common CAS registry number of (9003-01-4). Carbomers are synthetic high molecular weight polymers of polyacrylic acid that are cross-linked with either allylsucrose or allylethers of pentaerythritol.they contain between 56-68% of carboxylic groups appears as white/coloured, fully acidic hygroscopic powder, with a

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slight characteristic odour. They are soluble in water, after neutralization in ethanol (95%) and glycerine, disperse in water to form acidic colloidal solution of low viscosity that when neutralized produce highly viscous gel. These are the stable material which may be heated at temperature below 104^0C for up to two hours, without affecting their thickening efficiency, and are regarded as essentially safe excipients well tolerated up to 8gm/kg dose level. Carbomers are used mainly in liquid or semi-solid pharmaceutical formulations as a suspending or viscosity increasing agents. Carbomers grades with low residual benzene content, such as Carbopol 934P and 974P and low residual ethyl acetate levels, such as Carbopol 971P may be used in oral preparations, in suspensions, in tablets or sustained release formulations. The different grades of carbopol used in the study for optimization are carbopol 934P, carbopol 974P, carbopol 971P, and polycarbophil.

The drug, norfloxacin, in preliminary characterization for solubility and spectrophotometric quantification after identification, showed very poor solubility in water, sparingly soluble in chloroform, practically insoluble in acetone and alcohol but freely soluble in acetic acid. The drug melts at 227-228^{0}C and having absorption maxima (ëmax) at 277nm in acetate buffer pH 4. A standard calibration plot for spectrophotometric quantification of drug was developed by measuring the absorbance of 4µg/ml - 12µg/ml solution of drug, prepared in acetate buffer (pH 4). An optimized aqueous suspension of norfloxacin was prepared using soylecithin, hydroxyl propyl methyl cellulose, polyvinyl propylidone and Pluronic F68 by precipitation through sodium hydroxide. Mucoadhesion to the suspension was rendered by mixing various polymer gels of carbopol 971P, carbopol 974P, carbopol 934P, polycarbophil in 0.25%, 0.5%, 0.75% concentration to the optimized aqueous suspension of norfloxacin. The mucoadhesive suspension so prepared was characterized for drug polymer compatibility, viscosity, *in vitro* drug dissolution and permeation, and for bioadhession as parameter to know about the best optimum polymer out of different grades of cabopol used for the preparation of suspension. Test for biadhession was performed by measuring the detachment force *in vitro* and by the gamma scintigraphy using Tc^{99} labeled product filled in a capsule shell. The average percentage bioadhession determined by the detachment force quantification (Table 1) for different products was compared and interpreted along with gamma scintigraphy results. The *in vitro* drug release study was conducted as per USP guidelines and the results are plotted in Fig. 1. The gamma scintigraph demonstrated that mucoadhesive suspension of carbopol 971P was retained maximum in stomach for absorption, for 6 hours,

Table 1: Bioadhession profile of mucoadhessive suspensions of norfloxacin

Sr. No.	Product	Batch No.	Suspension : Gel ratio	% of bioadhesion
1.	Carbopol 971P	11	1:1	100
	(Gel conc.	12	2:1	97.76
	0.25%).	13	3:1	96.23
		14	4:1	93.10
2.	Carbopol 971P	15	1:1	100
	(Gel conc.	16	2:1	98.23
	0.5%)	17	3:1	97.15
		18	4:1	94.93
3.	Carbopol 971P	19	1:1	100
	(Gel conc.	20	2:1	100
	0.75%)	21	3:1	98.65
		22	4:1	96.28
4.	Polycarbophil	23	1:1	56.39
	(Gel conc.	24	2:1	24.23
	0.25%)	25	3:1	16.98
		26	4:1	10.43
5.	Polycarbophil	27	1:1	59.62
	(Gel conc.	28	2:1	28.67
	0.5%)	29	3:1	22.34
		30	4:1	16.92
6.	Polycarbophil	31	1:1	62.34
	(Gel conc.	32	2:1	31.92
	0.75%)	33	3:1	23.64
		34	4:1	18.58
7.	Carbopol 934P	35	1:1	98.52
	(Gel conc.	36	2:1	91.41
	0.25%)	37	3:1	89.39
		38	4:1	82.89
8.	Carbopol 934P	39	1:1	98.28
	(Gel conc.	40	2:1	95.64
	0.5%)	41	3:1	90.83
		42	4:1	84.42
9.	Carbopol 934P	43	1:1	99.53
	(Gel conc.	44	2:1	98.69
	0.75%)	45	3:1	95.43
		46	4:1	89.22
10.	Carbopol 974P	47	1:1	99.92
	(Gel conc.	48	2:1	96.54
	0.25%)	49	3:1	91.68
		50	4:1	84.23
11.	Carbopol 974P	51	1:1	100
	(Gel conc.	52	2:1	98.23
	0.5%)	53	3:1	95.69
		54	4:1	90.82
12.	Carbopol 974P	55	1:1	100
	(Gel conc.	56	2:1	99.63
	0.75%)	57	3:1	97.65
		58	4:1	95.34

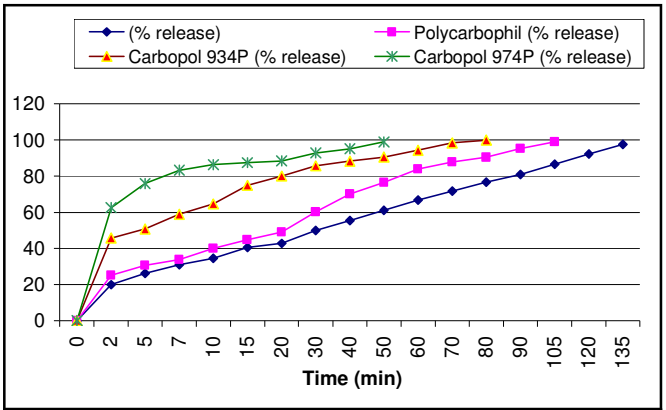

Fig. 1 : Drug release profile from mucoadhesive suspension of norfloxacin

compared to carbopol 934P. As 97.49% of drug is released in 135 minutes from carbopol 971P, the mucoadhesion of formulation to stomach for 6hrs is beneficial because increased residence time of the formulation. It can be concluded from the results of study that the reduction of particle size in precipitation method shows faster rate of dissolution, hence increased bioavailability. The higher gel concentration in formulation leads to increase in mucoadhesion and in reference to suspension: gel ratio, lower suspension: gel ratio favour better mucoadhesion. Keeping these entire variable in consideration the the polymers used along with drug, in suspension formulation shows retarded drug release in order Carbopol 971P > Polycarbophil > Carbopol 934P > Carbopol 974P. Results of gamma scintigraphy shows formulation retained in stomach for 6 hours which increases the residence time of formulation. Therefore Carbopol 971P is considered to be rationale grade of Carbopol polymer for the formulation of mucoadhesive suspension.

RESULTS AND DISCUSSION

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