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Influence of tamarind seed gum derivatives on the *in vitro* performance of gastro-retentive tablets based on hydroxypropylmethylcellulose

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The *in vitro* performance of gastro-retentive tablets containing metformin was investigated comprising work of adhesion (W), swelling and drug release. To measure W a method was adapted to apply shear stress horizontally. Tablets based on hydroxypropylmethylcellulose (HPMC) were compared with those containing a fraction of tamarind seed gum (TSG) or its derivatives instead of HPMC. Surprisingly, the TSG as well the derivatives investigated here were lowering W but they were increasing drug release rate and swelling of the tablets. TSG of carboxyl methyl type increased both dissolution and swelling significantly whilst W remained unchanged.

For gastro-retentive tablets, bioadhesion is often applied in combination with floating or swelling (Prinderre et al. 2011). To evaluate *in vitro* performance of the tablets described here adhesive and swelling properties were analyzed in parallel to drug release.

To measure the adhesive properties, a method derived from Metia and Bandyopadhyay (2008) was adapted applying shear stress horizontally and resulting in work of adhesion (W). To measure drug release, dissolution tests were performed and the time needed to release 60% of drug content ($t_{60\%}$) was evaluated. The swelling behavior (S) was expressed as increase in tablet thickness after $t_{60\%}$ hours and measured using a digital image analysis system as described earlier by Baumgartner et al. (2002).

The objective of this study was to investigate the *in vitro* performance of tablets containing hydroxypropylmethylcellulose (HPMC) as described earlier (Rajab et al. 2010) and tablets derived from this formula containing a fraction of tamarind seed gum (TSG) or its derivatives instead of HPMC. Two types of TSG derivatives were investigated, one carboxyl methyl ether (CMTG) and one hydroxypropyl ether (HPTG). All tablets of different formulas floated within 2 min and continued floating for 24 h.

As shown in the Table, W of the HPMC tablets was 7.87 J/m^2 and the admixture of TSG or its derivatives mostly did not change significantly this basic value. Surprisingly two types of TSG decreased W if they were embedded in a portion of 5%. HPTG decreased W in a portion of 3.33%. These results suggested weaker adhesive power of TSG and its derivatives versus HPMC and were quite contrary to results of Patel et al. (2009) describing TSG as strongly bioadhesive.

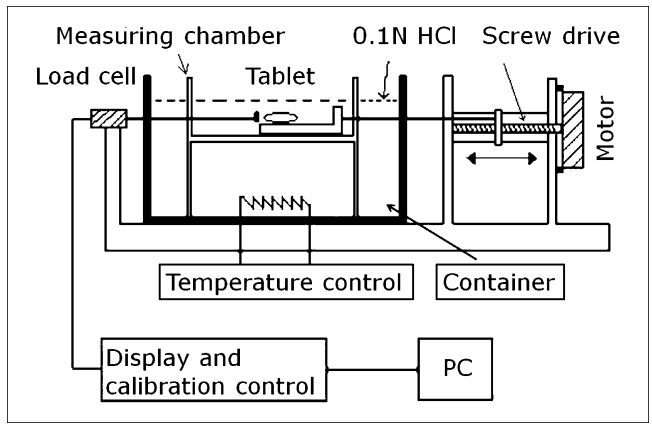

Fig.: Equipment to apply shear stress horizontally to the tablets whilst adhering to stainless steel, force measurement via load cell resulting in work of adhesion (W), derived from (Metia and Bandyopadhyay 2008).

60% of the metformin content was released within 3.81 h. No significant differences from this basic value of $t_{60\%}$ were noted for most of the formulas containing TSG or its derivatives. The carboxyl methyl derivative (CMTG) included in the formulas 1, 2, 3 increased $t_{60\%}$ significantly ($P < 0.02$), most if 3.33% CMTG was included, formula 2. This effect might be based on higher viscosity of this derivative (5,500 to 11,000 mPa*s) slowing down drug release rate as observed by Tadros (2010) for HPMC and admixtures of alginates.

The tablets of the formula 0 (HPMC only) achieved the 134% increase in tablet thickness (S) after $t_{60\%}$ h. The admixture of TSG enhanced swelling considerably. S was found significantly higher ($P < 0.05$) for all tablets containing CMTG or FGTG. For the tablets containing HPTG, only the formula 5 showed a significant increase in S but this was clearly behind that of the formulas containing CMTG or FGTG. However, the swelling of HPMC tablets can be modulated by incorporating auxiliary additives into tablet formulations (Matharu et al. 2010), and TSG evoked this effect highly probable.

The use of a fraction of TSG or its derivatives instead of HPMC in the tablets can help to adjust swelling and metformin release whilst adhesion of the swollen tablets remains unchanged.

Experimental

The tablets were made as described earlier (Rajab et al. 2010). Highly purified food grade TSG (FGTG, [TA400] CAS: 39386-78-2), carboxymethyl ether of TSG (CMTG, [HT-40] CAS 68551-04-2) and 2-hydroxypropyl ether of TSG (HPTG, [TG-30] CAS 68647-15-4) were all from SHIKIBO LTD. 3-2-6, Bingomachi, Chuo-ku, Osaka 541-8516 Japan.

The measurement device (Fig.) applied shear stress horizontally to the tablet whilst adhering to stainless steel. The load cell delivered one force measure (mN) per 9.6 ms with a deviation of ± 1.96 mN. The work of adhesion per unit area (W, J/m^2) was the quotient of the area (J) under a 3 min force versus distance profile and the contact area (m^2) (Thirawong et al. 2007).

To measure W, shear stress was applied horizontally at a constant speed (42 μm/s) to tablets after 2 h swelling in 0.1 HCl at 37 °C as shown in the Fig. To measure drug release, dissolution tests were performed using dissolution apparatus type 2 (USP 30, ERWEKA dissolution test, Heusenstamm, Germany), in 900 ml 0.1N HCl at 37 ± 0.5 °C and at 100 rpm. Sink condition was maintained for the whole experiment. The time needed to release 60% of the drug content ($t_{60\%}$) was evaluated (Rajab et al. 2010). The percent of tablet thickness after $t_{60\%}$ h in contact with 0.1 HCl at 37 °C relating to the thickness before was used as measure of S resulting from observations using a digital image analysis system (Baumgartner et al. 2002).

In order to compare the HPMC and TSG batches, unpaired two-tailed t-tests were carried out on all investigated quality parameters (W, $t_{60\%}$, S). Prior

Table 1: Work of adhesion (W), drug release ($t_{60\%}$) and percentage of swelling (S) of the formulas 0 to 9

No.	HPMC (%)	TSG code	Viscosity[1] (mPa*)	TSG (%)	W (J/m^2)	STD[2]	$t_{60\%}$ (hours)	STD[3]	S (%)	STD[2]
0	19.96	–	3,000 to 5,600	–	7.87	0.41	3.81	0.42	134.65	12.42
1	18.30	CMTG	5,500	1.66	8.56	0.55	5.17**	0.50	193.99*	12.59
2	16.63	CMTG	to	3.33	7.39	0.30	6.04**	0.30	210.07*	14.83
3	14.97	CMTG	11,000	4.99	5.87*	0.34	5.82**	0.29	210.91*	14.69
4	18.30	HPTG	5,100	1.66	7.71	0.80	3.79	0.29	162.20	12.78
5	16.63	HPTG	to	3.33	5.95*	0.53	3.70	0.24	173.18*	8.46
6	14.97	HPTG	6,300	4.99	7.06	0.23	3.47	0.27	156.85	13.76
7	18.30	FGTG	300	1.66	7.02	0.87	4.48	0.25	222.15*	11.98
8	16.63	FGTG	to	3.33	8.50	0.47	4.53	0.25	213.92*	12.10
9	14.97	FGTG	420	4.99	6.54*	0.05	4.40	0.25	215.40*	12.79

[1] 5% aqueous solution; STD[2], standard deviation (n = 3); STD[3], standard deviation (n = 6).
* significantly different from the corresponding result of formula 0 ($P < 0.05$)
** significantly different from the corresponding result of formula 0 ($P < 0.02$)

to the t-test the normal distribution of the data was confirmed using the Anderson–Darling normality test at significance level $\alpha = 0.05$; $t_{60\%}$ and S resulted from data fitted using Microsoft Excel (2007).

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