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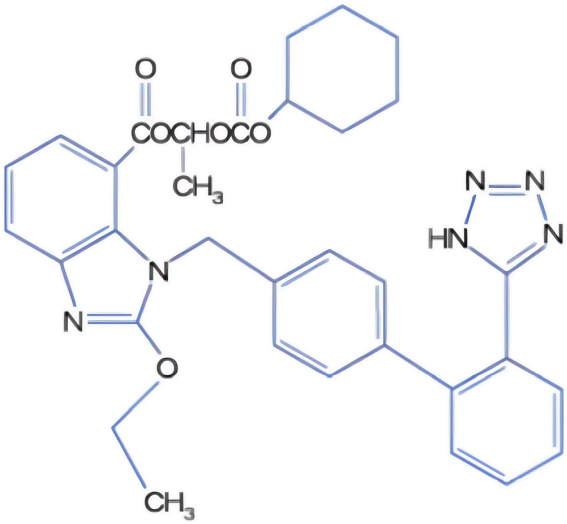
Creativity and Contribution

PHARMACEUTICAL NEWSLETTER

pH Independent Bi-layer Self-microemulsifying Tablets (SMETs) of Candesartan Cilexetil with Fujicalin® and Neusilin®

INTRODUCTION

CANDESARTAN CILEXETIL (CDC)



An angiotensin II receptor antagonist is a prodrug which gets converted to active drug Candersartan during absorption from the gastrointestinal tract.

The conventional CDC tablets have a significantly low bioavailability of approximately 14% after oral administration.

SELF-MICROEMULSIFYING DRUG DELIVERY SYSTEM (SMEDDS)

Self-microemulsifying Drug delivery system (SMEDDS) approach is becoming a common practice to enhance oral bioavailability of poorly water soluble drugs. To produce tablets of SMEDDS and to have a desired dissolution profile is considered one of the most difficult tasks for a formulator. Through several publications and commercial products, Neusilin® and Fujicalin® have proved to be some of the best adsorbent carriers available in the industry today.

In this newsletter, we summarized a recent study by Sohn et al, Pharmazie 67: 917–924 (2012). where a-pH-independent fast release bi-layer self-microemulsifying tablets (SMETs) of Candesartan Cilexetil were prepared using Neusilin®and Fujicalin® as adsorbent carriers.

FORMULATION: THE PREPARATION WAS DONE IN 2 STEPS.

STEP 1: PREPARATION OF SMEDDS

SMEDDS was prepared using Capryol90™, Tween® 80, and tetraglycol in the ratio 5:35:60. This ratio was arrived at after several trials for dispersibility, solubilizing capacity, smallest particle size of micro-emulsion and polydispersibility index (PDI).

STEP 2: PREPARATION OF SMET

SMEDDS was adsorbed on to solid carrier materials- Neusilin® UFL2, Fujicalin®, and Aeroperl® 300. Tablets were prepared as per composition given in Table 1.

Table 1: Tableting formulation for development of self-microemulsifying tablets(SMET)

SMET Formulation	SMEDDS (µL)	Fujicalin® (Mg)	Neusilin® UFL2 (Mg)	Aeroperl® 300 (Mg)	Pearlitol (Mg)	Polyplasdone (Mg)	Mg. Stearate (Mg)	Hardness* (kp)
Fujicalin®-based	123	250			100.75	25	1.25	3.13+0.18
Neusilin®-based	123		117.9		232.85	25	1.25	5.55±0.89
Aeroperl®-based	123	125		142.3	208.45	25	1.25	5.30±1.38
Bi-layer First Layer	61.5		58.95		50.375	12.5	0.625	4.87±0.75
Bi-layer Second Layer	61.5				116.425	12.5	0.625	
	*Hardness data are expressed as mean ± SD (n=3). All formations contain 8 mg of Candesartan Cilexetil.							

DISSOLUTION PROFILE

Release of CDC from **Fujicalin®** SMET is comparable to CDC release from liquid SMEDDS (fig.1) in pH 1.2. While release of CDC from **Neusilin® UFL2** SMET is comparable to CDC release from liquid SMEDDS (fig.2) in pH 6.5.

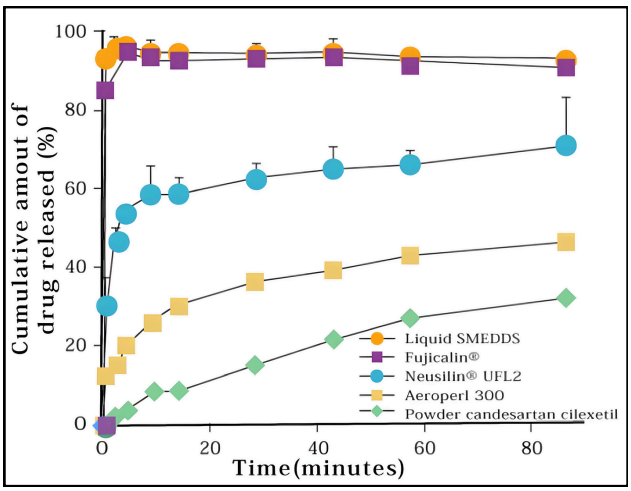


Fig.1: Dissolution profiles of CDC in SMETs in simulated gastric juice(pH 1.2) with 0.5% Tween® 20. Data expressed as mean ± SD (n=3)

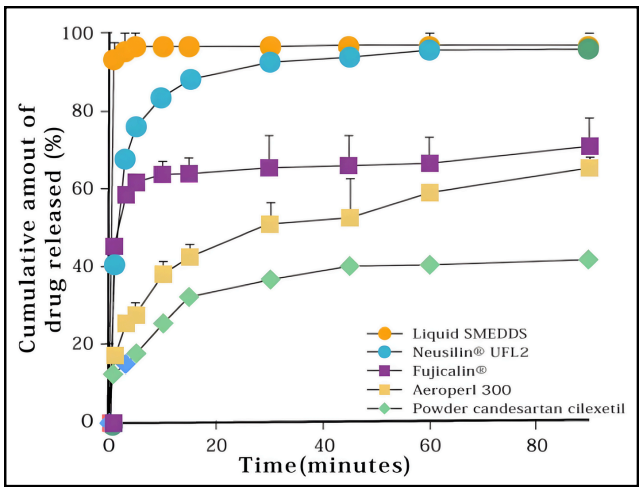
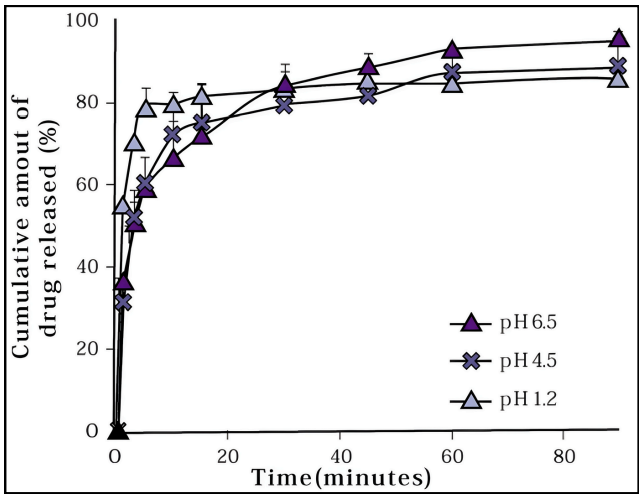


Fig.2: Dissolution profiles of CDC in SMETs in 0.05M phosphate buffer (pH 6.5) with 0.35% Tween® 20. Data expressed as mean ± SD (n=3)

As seen in the above two graphs, the release of CDC from Aeroperl® 300 is comparatively low even though its specific surface area (300 m^2/g) is similar to that of **Neusilin® UFL2**.
This could be due to the entrapment of CDC in the pores of Aeroperl® 300 through which the drug must migrate.



DATA ARE EXPRESSED AS MEAN ± SD (N=3)

Fig.3: Dissolution profiles of CDC in self-microemulsifying bi-layer tablets at different conditions (pH 1.2, pH 4.5 and pH 6.5) containing 0.35% Tween 20.

After understanding the dynamics of **Fujicalin®** SMET and **Neusilin® UFL2** SMET, a bi-layer tablet consisting of **Fujicalin®** in the first layer and **Neusilin® UFL2** in the second layer was prepared.
The composition of the bi-layer was as mentioned in Table 1. The dissolution profile of the bi-layer SMET is as shown in Fig. 3.

CONCLUSIONS

Fujicalin® has high water adsorption capacity and erodes quickly at pH 1.2, thereby releasing CDC at a rate comparable to that of liquid SMEDDS. Whereas **Neusilin® UFL2** has a very small particle size, high surface area, and high oil adsorption capacity.
The release of CDC at pH 6.5 from **Neusilin® UFL2**-based SMET is comparable to that of liquid SMEDDS. Thus, by preparing bi-layer SMET of CDC with **Fujicalin®** and **Neusilin® UFL2**, it is possible to get immediate release of CDC, which is independent of the pH of GIT.

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CONTACT US

India
AstaReal (India) Private Limited
(A Fuji Chemical Group Company)
Unit No. 606/6th floor, Sunteck
Crest, Behind Mukund Hospital,
Near Leela Business Park,
Andheri East, Mumbai – 400059
Tel. +91-22-62369998
Email: pharma@fujichemical.co.jp

Europe
AstaReal AB
(A Fuji Chemical Group Company)
Forumvägen 14, Level 16,
131 53, Nacka, SWEDEN
Tel. +46-8-570-139-50
Email: pharma@fujichemical.co.jp

USA
Fuji Chemical Industries USA, Inc.
3 Terri Lane, Unit 12
Burlington, NJ 08016 USA
Tel. +1-609-386-3030
Email: contact@fujichemicalusa.com
www.fujichemicalusa.com

Japan
Fuji Chemical Industries Co., Ltd.
Shibakoen Ridge Building 2nd Floor,
1-8-21 Shiba Koen, Minato-ku,
Tokyo 105-0011 JAPAN
Tel. +81-3-3437-2350
Fax: +81-3-3437-2347
Email: pharma@fujichemical.co.jp
www.fujichemical.co.jp/english

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