

An In Vitro Analysis of Disintegration Times of Different Formulations of Olanzapine Orodispersible Tablet: A Preliminary Report

David Hobbs · Jamie Karagianis ·
Tamas Treuer · Joel Raskin

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Abstract

Background Orodispersible tablets (ODTs) are tablet or wafer forms of medication that disintegrate in the mouth, aided only by saliva. ODTs rely on different fast dissolve/disintegration manufacturing technologies.

Objectives Disintegration time differences for several olanzapine ODT forms were investigated. Risperdal M-Tab[®] was included as a non-olanzapine ODT comparator.

Research Design and Methods Eleven olanzapine ODT examples and orodispersible risperidone strengths were evaluated in vitro for formulation composition, manufacturing method, disintegration and dissolution characteristics,

and formulation differences in comparison with freeze dried Zydis[®] ODT. Automated dissolution test equipment captured ODT dissolution rates by measuring real-time release of active ingredient. A high-speed video camera was used to capture tablet disintegration times in warm simulated saliva. **Main Outcome Measure** The main outcome measure was the disintegration and dissolution characteristics of the ODT formulations.

Results The ODT manufacturing method was associated with time to disintegrate; the fastest were freeze dried tablets, followed by soft compressed tablets and then hard/dense tablets. Olanzapine Zydis[®] was the only ODT that completely disintegrated in less than 4 s for all strengths (5, 10, 15, and 20 mg), followed by 5-mg Prolanz FAST[®] (12 s) and then risperidone ODT 4 mg (40 s). Reasons for slow dissolution of the olanzapine generics may include low product potency, excipient binding, excipient solubility, active ingredient particle size and incomplete disintegration.

Conclusions Differences in the formulation and manufacturing process of olanzapine ODTs appear to have a strong influence on the disintegration time of the active compound; differences that may potentially impact their use in clinical practice.

This work was conducted when JK was an employee of Eli Lilly.

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D. Hobbs (✉)
Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN
46285, USA
e-mail: hobbsdg@lilly.com

J. Karagianis
Waypoint Centre for Mental Health, 500 Church St,
Penetanguishene, ON L9M 1G3, Canada

J. Karagianis
Department of Psychiatry, University of Toronto, Toronto,
Canada

T. Treuer
Eli Lilly and Company, Madach I. u. 13-14, Budapest 1075,
Hungary

J. Raskin
Eli Lilly Canada Inc., 3650 Danforth Avenue, Toronto, ON M1N
2E8, Canada

1 Introduction

The treatment of mental disorders usually requires prolonged pharmacotherapy in order to resolve the current episode and reduce the risk for recurrence of symptoms, while addressing the challenges of low compliance in the long term. Such prolonged therapy requires considerable commitment on the part of patients to take their medication as prescribed. Medication compliance is often challenging

among psychiatric patients, including those with schizophrenia or bipolar disorder; this can be associated with poor long-term outcomes and, ultimately, treatment failure [1].

A greater understanding of patients' preferences for new formulations of treatment is central to current models of shared patient–doctor decision making, and has gained considerable interest in scientific research for orodispersible formulations of antidepressants and antipsychotics [2]. The effectiveness of the antipsychotic drug olanzapine classic oral tablet in the treatment of patients with schizophrenia has been widely investigated in several randomized, controlled trials, and observational studies [3–7] and in several meta-analyses [8, 9].

In recent years, more clinical attention has been paid to oral dispersible tablet formulation of medications [10]. Lyophilized (freeze dried), orally disintegrating olanzapine is a rapid dissolving formulation of olanzapine that disintegrates in saliva almost instantaneously. The formulation was developed as a convenient, easy to ingest and potentially adherence-enhancing alternative to the standard olanzapine coated tablet. Pharmacokinetic studies have shown that the olanzapine orodispersible tablet (ODT) is bioequivalent to olanzapine standard tablet with the same rate and extent of bioavailability [11]. Clinical studies have shown that olanzapine ODTs and standard olanzapine tablets have similar efficacy and tolerability profiles; however, olanzapine ODTs appear to have a number of advantages over olanzapine standard tablets in terms of adherence, patient preference and reduction in nursing burden [2, 12, 13].

Olanzapine ODTs may be useful for patients who have difficulty swallowing standard tablets; those with poor insight who may try to cheek or spit out their medication; those who need to have their ingestion verified but who do not want an injection; or those who prefer this formulation for other reasons. There are many generic olanzapine orodispersible formulations, but their relative disintegration and dispersion times have never been studied to our knowledge. Variation in dispersion times might be expected, depending on the different fast dissolve/disintegration technologies used to manufacture the tablets and/or the disintegration test used to evaluate them. Olanzapine Zydis[®] (also known as Velotab[®]) is manufactured by Catalent Pharma Solutions (Somerset, NJ, USA), and is made by a freeze drying process that provides a low-density, highly porous structure that readily disintegrates in the oral cavity. Although bioequivalence is accepted for generic ODTs, the time it takes for an ODT to disintegrate and dissolve in the oral cavity may potentially impact clinical parameters such as patient acceptance and adherence to treatment.

For olanzapine Zydis[®] ODT, the elapsed time for initial and complete disintegration was measured in two small

in vivo studies [14, 15]. However, these studies used different methods: one took the first measurement of initial disintegration at 15 s, while the other took the first measurement at 5 s. It is desirable to compare disintegration times among different products using the same methodology. Given the obvious challenges of standardizing in vivo assessments, the objective of our current in vitro comparison was to investigate in vitro disintegration time and dissolution rate differences of various generic formulations of olanzapine ODT relative to olanzapine Zydis[®] in simulated saliva. We also compared the chemical and physical properties of each ODT and measured in vitro disintegration time for risperidone ODT [16] as a comparator.

2 Materials and Methods

All types of olanzapine ODT that could be obtained were evaluated (Table 1). Eleven different examples were filmed to determine disintegration times, and all were evaluated for manufacturing method, dissolution characteristics and formulation differences, including the freeze dried Zydis[®] formulation of olanzapine ODT and risperidone ODT. A Canon XHL1 HD camera (Canon, Tokyo, Japan) was used to capture a 3-min disintegration event for each ODT product added to 30 mL of non-agitated 37 °C (initial temperature) simulated saliva solution in a 10-cm Petri dish. Disintegration was defined as the time it took a tablet to reach full dispersion after addition to the artificial saliva (see Table 2 for the formulation, based on formulations described in Giannola et al. [17] and Gal et al. [18]). Drug product excipient data were obtained from published product literature. Dose form and manufacturing method (compressed tablet, lyophilized wafer) were determined by microscopic/visual observation.

Dissolution testing used a USP Apparatus #2, DISTEK DISBA0045 and DISBA0046 with an Opt-Diss UV fiber optic SPEC0088 attachment (Distek Inc., North Brunswick, NJ, USA). The system quantified the solubilized antipsychotic in 500 mL of 37 °C simulated saliva every 10 s for 6 min, and then every minute for 14 min, with paddle speeds of 20 or 30 rpm to simulate the oral cavity environment [16] (Table 3). Agitation was then increased 150 rpm for an additional 16 min to release all available olanzapine. Olanzapine active ingredient standard was used to calibrate the system, and dissolution was repeated a minimum of three times. The Distek dissolution apparatus was calibrated with three standards for each of the 12 probes (two dissolution baths with six vessels each) and a standard absorbance curve was calculated for each probe. If the relative standard deviation was too high, the probe was not used. Care was taken to randomize the analysis within the vessels available and thus provide assurance of

Table 1 Drug names and manufacturing information

Commercial name	Manufacturer	Strength (mg)	Manufacturing method	Expiration	Lot number	Country of origin	Distributor
Risperdal M-Tab [®]	Janssen Pharmaceuticals Inc.	2	Freeze dried tablet	06/2012	0JG018	USA	Janssen Pharmaceuticals Inc.
Risperdal M-Tab [®]	Janssen Pharmaceuticals Inc.	4	Freeze dried tablet	01/2012	0BG1274	USA	Janssen Pharmaceuticals Inc.
Novo-Olanzapine OD [®]	Teva Pharmaceutical	5	Molded tablet	01/2013	03400081	Canada	Nova Pharm
Olanzapine FT [®]	ABL Pharma	5	Compressed tablet	02/2012	B0683A	Chile	ABL Pharma Peru SAC
Olanzapine ODT [®]	Sandoz Canada Inc.	5	Compressed tablet	03/2012	0000876	Canada	Sandoz Canada Inc.
Olaxinn [®]	Ali Raif Ilac San. A.s. (ARIS)	5	Compressed tablet	04/2012	10040845	Turkey	Generica Ilac San.ve Tic.
pms-Olanzapine ODT [®]	PharmaScience Inc.	5	Compressed tablet	07/2011	C000303	Canada	PharmaScience Inc.
Prolanz FAST [®]	Procaps S.A., Barranquilla	5	Compressed tablet	06/2012	0062447	Columbia	NA
Zolrix [®]	KRKA Polska Sp., Varsava	5	Compressed tablet	01/2012	P14110-0110	Poland	Salus, Ljubljana, d.d.
Zyprexa [®] Zydis [®]	Eli Lilly and Company	5	Freeze dried wafer	06/2013	1076944	Britain	Eli Lilly and Company
Anzapine ORO [®]	Okasa Pharma Pvt. Ltd	10	Compressed tablet	08/2010	S88053	India	Laboratoire BIO VITAL
Lanzaprex [®]	El Kendi Industrie du Med.	10	Compressed tablet	09/2012	L10C2	Algeria	NA
Olanzapine FT [®]	ABL Pharma	10	Compressed tablet	02/2012	B0735A	Chile	ABL Pharma Peru SAC
Prolanz FAST [®]	Procaps S.A., Barranquilla	10	Compressed tablet	04/2012	0041462	Columbia	NA
Tanssel D [®]	Okasa Pharma Pvt. Ltd	10	Compressed tablet	06/2011	SJ9016	India	Biocross S.A. Guatemala
Zyprexa [®] Zydis [®]	Eli Lilly and Company	10	Freeze dried tablet	06/2013	1076944	Britain	Eli Lilly and Company
CO Olanzapine ODT [®]	Cobalt Pharmaceuticals	15	Compressed tablet	06/2012	BX411	Canada	Cobalt Pharmaceuticals
pms-Olanzapine ODT [®]	PharmaScience Inc.	15	Compressed tablet	07/2011	C000305	Canada	PharmaScience Inc.
Zyprexa [®] Zydis [®]	Eli Lilly and Company	15	Freeze dried tablet	04/2013	1058967	Britain	Eli Lilly and Company
Novo-Olanzapine OD [®]	Teva Pharmaceutical	20	Molded tablet	11/2012	93440011	Canada	Nova Pharm
Olaxinn [®]	Ali Raif Ilac San. A.s. (ARIS)	20	Compressed tablet	04/2012	10040848	Turkey	Generica Ilac San.ve Tic.
Olanzapine ODT [®]	Sandoz Canada Inc.	20	Compressed tablet	12/2011	0000012	Canada	Sandoz Canada Inc.
Zolrix [®]	KRKA Polska Sp., Varsava	20	Compressed tablet	10/2011	P14065-1009	Poland	Salus, Ljubljana, d.d.
Zyprexa [®] Zydis [®]	Eli Lilly and Company	20	Freeze dried tablet	04/2013	1067672	Britain	Eli Lilly and Company

ODT orodispersible tablet

NA not available

Table 2 Simulated saliva formulation

Ingredient	Grams/liter of purified water
Sodium chloride (NaCl)	0.126
Potassium chloride (KCl)	0.964
Potassium thiocyanide (KSCN)	0.189
Potassium phosphate monobasic (KH ₂ PO ₄)	0.655
Urea	0.200
Sodium sulfate (Na ₂ SO ₄ 10H ₂ O)	0.763
Ammonium chloride (NH ₄ Cl)	0.178
Calcium chloride dihydrate (CaCl ₂ 2H ₂ O)	0.228
Sodium bicarbonate (NaHCO ₃)	0.631

Table 3 Orodispersible tablet dissolution conditions [19]

Parameter	Equipment/Measure
Dissolution apparatus	DISBA0045, DISBA0046 (Distek 6100)
Configuration	Paddles (USP apparatus 2)
Temperature	37 °C
Medium	Simulated saliva
Volume	500 mL
Rotational speed	30 rpm
Analysis	SPEC0088 (Distek Opt-Diss Fiber Optic UV dissolution system)
Wavelength	255 nm (with blank subtraction at 330 nm) for olanzapine 276 nm (with blank subtraction at 330 nm) for risperidone
Frequency of readings	Every 10 s from 0 to 6 min Every 1 min from 6 to 20 min Then change paddle speed to at least 150 rpm and take one reading at 30 min and at 90 min

comparable results of tests performed in triplicate on each generic tablet. Initial disintegration was quick and difficult to differentiate among some products, so the time to first measurable concentration of active ingredient in the dissolution media (simulated saliva) was used as a proxy, since the onset of dissolution is normally preceded by disintegration.

3 Results

3.1 Disintegration Times (Time Taken to Reach Full Dispersion)

We found that the method of ODT manufacture (see Table 1 for manufacturing details for all compounds tested) had the greatest influence on the time for disintegration; in general, the fastest were freeze dried tablets, then

soft compressed tablets and then hard/dense tablets. Olanzapine Zydis[®] was the only ODT that completely disintegrated in less than 4 s for all strengths (5, 10, 15, and 20 mg; Table 4). The second fastest disintegration time was Prolanz FAST[®] (5/10 mg; 12 s), followed by risperidone (4 mg; 40 s).

In the agitated aqueous media of the dissolution vessel (rather than the sedentary environment of the Petri dish just described), both olanzapine Zydis[®] and risperidone ODT disintegrated immediately upon coming into contact with aqueous media; however, the active compound (olanzapine) in the Zydis[®] tablets dissolved faster in the simulated saliva media (pH 6.8) than the risperidone in the risperidone ODTs. Surprisingly, risperidone 2-mg ODT disintegrated slower than the 4-mg with double the mass, and was potentially influenced by the shape and density of the tablet. Other products varied in their disintegration characteristics, but essentially remained as a clump that did not always fully disperse when physically agitated after 3 min of standing without mixing. Compressed tablets consistently had a higher amount of visible residue at the end of the 3-min evaluation period.

3.1.1 Dissolution Times (Release of Active Product)

Using time to dissolution as a proxy for disintegration, several generics required 20 s or more to initiate release of the drug substance (Table 5) and required both increasing the agitation rate, and additional time (~30 min) to maximize dissolution. In this evaluation, only four of the drug products tested released more than 80 % of the active ingredient within the first 10 min. Release for all but Zo-lrix[®] was around 90 % or above after applying 150 rpm for 10 min at the end of the analysis.

3.1.2 5-mg Olanzapine and 4-mg Risperidone ODTs

Figures 1 and 2 are a summary of the 5-mg data at 30-rpm paddle speed for the first 3 min and first 30 min, respectively. When examining the first 3 min (Fig. 1) of the dissolution profile, the olanzapine Zydis[®] formulation is the first to release active compound, with dissolution over 30 % in less than 60 s, twice as fast as the 4-mg risperidone ODT. The Prolanz FAST[®] 5-mg formulation is also rapid and after 1 min had higher, although more variable, release (Fig. 1). Three samples (olanzapine Zydis[®], Prolanz FAST[®], and Novo-Olanzapine OD[®]) were run again at the lower agitation speed to explore potential differences between the products; at 20 rpm, only olanzapine Zydis[®] disintegrated instantly, and Prolanz FAST[®] had a noticeable delay in the low-agitation environment. Novo-Olanzapine OD[®], a molded tablet, also had a faster dissolution profile than the remainder of the samples (Fig. 1).

Table 4 Tablet excipients and disintegration

Commercial name and dose	Excipients	Disintegration observations
ABL Olanzapine FT [®] 10 mg; Zapinex FT [®] 5, 10 mg	Lactose monohydrate, hydroxypropyl cellulose, crospovidone, magnesium stearate, glycerin diacetate, colloidal silicon dioxide, microcrystalline cellulose, polyethylene glycol 8000, mint powder	Yellow and red, compressed tablet, stops swelling in media after 55–75 s, disintegration >180 s ^a
Anzapine ORO [®] 10 mg	Lactose monohydrate, hydroxypropyl cellulose, sodium cyclamate, magnesium stearate, talc	Compressed tablet, stops swelling in media after 85 s, coarse disintegration >180 s ^a
CO Olanzapine ODT [®] 15 mg	Not available	Pale yellow, round, compressed tablet, disintegration >180 s ^a
Lanzaprex [®] 10 mg	Lactose, crospovidone, hydroxypropyl cellulose, aerosil, talc, magnesium stearate, mint aroma	Compressed tablet, stops swelling in media after 44 s, disintegration complete at <180 s ^b
Novo-Olanzapine OD [®] 5, 15, 20 mg	Mannitol, sodium starch glycolate, dextrose, flavoring, (tartrazine), FD&C yellow #5 aluminum lake	Yellow (5), pink (15), and blue (20), round, compression molded tablet fully wetted in 5 s, disintegrated in <180 s ^b
Olaninn [®] 5, 20 mg	Crospovidone, lactose monohydrate, colloidal silicon dioxide, hydroxypropyl cellulose, talc, magnesium stearate, mint powder	Yellow, round, compressed tablet fully wetted in 5–9 s, disintegrated in <180 s ^b
pms-Olanzapine ODT [®] 15, 5 mg	Aspartame, colloidal silicon dioxide, crospovidone, guar gum, magnesium stearate, mannitol, microcrystalline cellulose, pregelatinized starch, sodium lauryl sulfate	Yellow, round, compressed tablet fully wetted in 5 s, disintegrated in <180 s ^b
Prolanz FAST [®] 5, 10 mg	Lactose monohydrate, hypolose, crospovidone, microcrystalline cellulose, magnesium stearate	Red, 5/10-mg, compressed tablet, disintegrated in 7–12 s, coarse dispersion at 180 s
Sandoz Olanzapine ODT [®] 20 mg	Colloidal silicon dioxide, crospovidone, flavoring, mint powder, hydroxypropyl cellulose, lactose monohydrate, magnesium stearate, talc	Compressed tablet, stops swelling in media after 85 s, disintegrated at 180 s
Zolrix [®] 20 mg	Mannitol, microcrystalline cellulose, crospovidone, hydroxypropyl cellulose, aspartame, calcium silicate, magnesium stearate	Compressed tablet, disintegrated in media after 25 s, coarse dispersion at 180 s
Zyprexa [®] Zydis [®] 5, 10, 15, 20 mg	Mannitol, aspartame, gelatin, preservatives	Fully dispersed in 4 s
Risperdal M-Tab [®] 2, 4 mg	Colloidal silicone dioxide, hypromellose, lactose, magnesium stearate, microcrystalline cellulose, propylene glycol, sodium lauryl sulfate, corn starch, colorant	Red, 4-mg, round wafer, fully wetted at 3 s, disintegrated in 40 s, 2-mg pillow is slower and lumps

ODT orodispersible tablet

^a Disintegration was not complete at 180 s. When the Petri dish was stirred, there was clearly core material still intact

^b Disintegration was a slow erosion of the core tablet, and it was not obvious when disintegration was complete; yet when stirred at the end of 180 s, there was no evidence of tablet core material (lump). In these cases, the tablet was said to have disintegrated in <180 s, but significantly more slowly than Zydis[®] or risperidone (minutes instead of seconds)

As shown in Fig. 1, olanzapine Zydis[®] is the first to initiate disintegration and shows a steady rate of dissolution, whereas some of the generic ODTs were well below 100 % even at the 30-min dissolution time point (Fig. 2).

3.1.3 10-mg Tablets

The Prolanz FAST[®] formulation has a quick dissolution time, but shows a longer delay to catch up to the Zydis[®] formulation, taking 2 min before they are equivalent (data not shown; see Figs. 1, 2 for 5-mg dose profiles). At a lower agitation rate of 20 rpm, olanzapine Zydis[®] 10 mg still has the fastest dissolution rate in the first 3 min, and olanzapine Zydis[®] dissolution is not significantly affected by dosage strengths (5, 10 mg). However, the Prolanz

FAST[®] dissolution rate is affected by the increased mass of the tablet.

3.1.4 15-mg Tablets

At 20 min, the generic ODTs released less than 60 % of active compound, while olanzapine Zydis[®] released 95 %. At the 90-min time point, and with increased agitation, the generic ODTs reached 96–112 % release.

3.1.5 20-mg Tablets

The olanzapine Zydis[®] ODT formulation is the fastest to disintegrate and dissolve. With a longer dissolution time (90 min) and increased agitation, all products were close to

Table 5 Time to first measurable concentration at 30 rpm

Product name	Time, percentage released (s, %) by formulation strength			
	5 mg	10 mg	15 mg	20 mg
ABL Olanzapine FT [®]	0, 1	10, 1 ^a 40	–	–
Anzapine ORO [®]	–	30, 1	–	–
ARIS Olaxinn [®]	0, 1 ^a 5	–	–	20, 1
CO Olanzapine ODT [®]	–	–	20, 2 ^a 25	–
Lanzaprex [®]	–	15, 1 ^a 35	–	–
Novo-Olanzapine OD [®]	10, 3 ^a 15	–	–	30, 1
pms-Olanzapine ODT [®]	10, 2 ^a 15	–	20, 1	–
Prolanz FAST [®]	20, 8	10, 2 ^a 25	–	–
Sandoz Olanzapine ODT [®]	20, 1 ^a 25	–	–	20, 1 ^a 25
Tanssel D [®]	–	30, 1 ^a 35	–	–
Zolrix [®]	0, 1 ^a 5	–	–	20, 1 ^a 25
Zydis [®]	0, 4 ^a 5	5, 7	0, 1 ^a 5	0, 1
Risperdal M-Tab ^{®b}	10, 2	–	–	–

ODT orodispersible tablet

^a Unadjusted time as per graph. Some graphs did not start at zero

^b Data shown are for the 4-mg dose

Fig. 1 Summary of 5-mg dissolution data at 30 rpm, up to 3 min. ODT orodispersible tablet

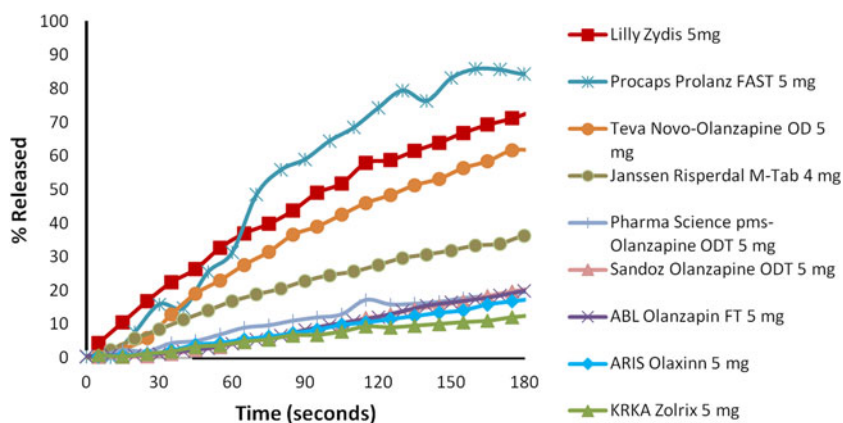
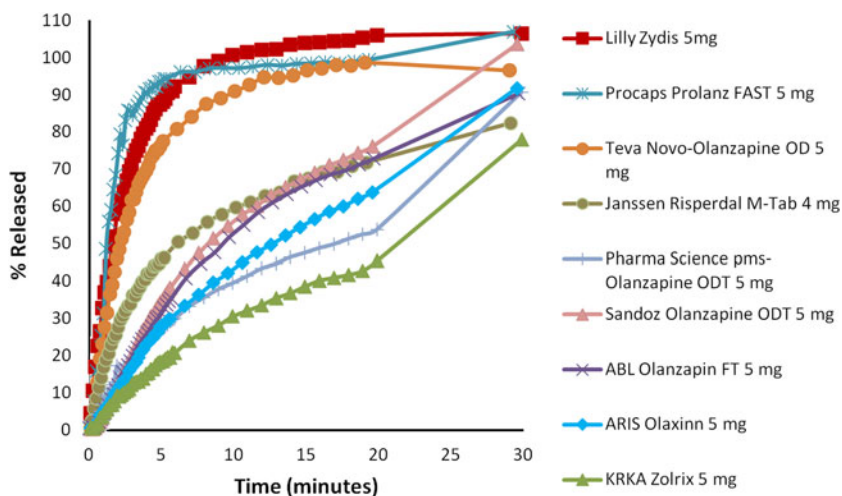


Fig. 2 Summary of 5-mg dissolution data at 30 rpm, up to 30 min. ODT orodispersible tablet



100 % released at the final time point. The freeze dried ODT dissolution profiles are very similar regardless of the tablet mass or active ingredient content. Generic ODT formulations using conventional compression or molding methods of manufacture were significantly slower to dissolve as the mass of the tablet increased.

4 Discussion

Based on our results, we found potentially important differences between ODT formulations manufactured with different technologies. The simulated saliva in vitro dissolution test may be considered a proxy for the disintegration process in a patient's mouth because it mimics the oral cavity environment and solutions. Differences in ODT formulation, manufacturing process, and tablet mass are associated with different disintegration times, which may have a potential impact on their use in clinical practice. Different disintegration times and tablet residue could influence mouth feel and the ability to swallow unaided by fluids, which could, in turn, influence adherence to treatment.

It is important to note that several generic tablet disintegration rates are slow enough to permit 'cheeking' and expectoration of the medication. Surreptitious rejection of medication by patients occurs sometimes in clinical practice [15]. If a tablet is swallowed and the pH becomes more acidic, the olanzapine will dissolve more rapidly than in the more neutral pH of saliva; however, the time for complete disintegration may be no better than in the mouth. Clinicians need to be aware of the potential differences among products, because it could differentially influence the success of this behavior. The use of polymeric excipients, which swell in water to speed disintegration, may inhibit rapid and complete dissolution of the active ingredient in some formulations.

There are three possible explanations for the low final dissolution values (<90 %) after 30 min in the dissolution bath: (1) olanzapine is not very soluble in aqueous solutions close to pH 7, and in these formulations, active pharmaceutical ingredient particle size may make a difference; (2) the drug is trapped or bound to excipients; or (3) analytical interference from the excipients. At 20 min, generics released less than 60 %, while olanzapine Zydis[®] released 95 %. With the longer time point (90 min), they reached 96–112 % release. Generic ODT formulations using loosely compressed tablets had relatively fast and/or coarse disintegration but slow dissolution. Olanzapine Zydis[®] (a freeze dried tablet) was the fastest disintegrating ODT formulation and exhibited the most effective dissolution curve of all the tablet strengths tested, regardless of potency. The investigated generic olanzapine ODT

products required more than 30 s to dissolve even 10 % of the active ingredient when compared with olanzapine Zydis[®] ODT, which could release approximately 25 % in the same time period.

Generic ODT products use different manufacturing platforms: direct compression; molded tablets; uncoated tablets; and some with pigment colorants. Risperdal M-Tab[®] and olanzapine Zydis[®] tablets may have similar disintegration rates, but the Zydis[®] ODT dissolved at twice the speed (likely due to the differences in active ingredient solubility in artificial saliva). In our tests, the smaller mass of the 5-mg olanzapine ODTs may facilitate the observed shorter disintegration and dissolution times versus the larger 20-mg tablets. Generic olanzapine ODT formulations incorporate water expansive polymers that appeared in the dispersion as a coarse insoluble residue, which may explain slow dissolution rates. After 5 min, some generic forms of olanzapine ODT almost match the dissolution rate of Zydis[®] but do not realize 100 % release.

There are some limitations of our experiments. The in vitro disintegration times may not be identical to in vivo disintegration times, and the small number of generic drug tablets available to the investigation did not permit statistical analysis.

5 Conclusions

The in vitro artificial saliva disintegration and dissolution tests are a proxy for the disintegration process in a patient's mouth. Tablet orodispersibles are consistently slower to disintegrate and release drug substance than lyophilized wafers. Compared with olanzapine Zydis[®] ODT, generic olanzapine ODT formulations of soft compressed tablets incorporate water expansive polymers that appeared in the dispersion as a coarse insoluble residue, which may explain their slow dissolution rates. Furthermore, in a direct comparison between risperidone ODT and olanzapine Zydis[®], orodispersible drugs with similar manufacturing methods (lyophilization), it is evident that, even though disintegration rates are similar, the risperidone is not as soluble in artificial saliva as is olanzapine. By using these test methods, differences in the formulation and manufacturing process of ODTs were seen to have a strong influence on the disintegration and dissolution of the drug products; differences that may potentially affect their use in clinical practice.

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format at the WFSBP Congress 2011, Prague, 29 May–2 June 2011 [20].

Author contributions All authors were involved in the development and writing of this manuscript, and all approved the final version.

Conflict of interest David Hobbs, Tamas Treuer, and Joel Raskin are employees of Eli Lilly and Company, the manufacturer of olanzapine. Jamie Karagianis is a former employee of Eli Lilly and Company. Lilly laboratories conducted the main tests, and all authors participated in the design of the experiment and in the interpretation of the results.

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