RIGGTEK
Dissolution Test Systems

DISSOLUTION MEDIA DEGASSING EFFICIENCY INVESTIGATION WITH DISSOPREP

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1 Introduction

There are many questions around degassing efficiency of the DissoPrep dissolution media delivery station compared to the recommendation of the USP[1]. USP (chapter 711) proposes a reference method[2] for degassing of the dissolution media, mainly with parameters like “degassing while stirring heated media under vacuum”. The vacuum is not defined, also not the storage condition. Other validated deaeration / degassing techniques are permitted[3],[4],[5]. The USP Certificate for the prednisone tablets includes a degassing recommendation where the vacuum is defined as < 100 mbar while additional 5 min and the media temperature not under 37°C.

2 Experimental

We have investigated in several degassing tests while the parameters temperature and vacuum (absolute pressure defined) and also “additional degassing time” are the main variables. Stirring is performed through a magnetic bar in the storage tank which is digitally driven and software monitored in its function. Duration of degassing is dependent of the reproducible filling time of the storage tank and the additional degassing time which can be selected.

3 Results and Discussion

The results are listed in the table below (where the results of DissoPrep X15 are equivalent). There are 18 tests, the last 2 are performed with extended degassing times. The measurements are performed with reasonable precision. Nevertheless the common uncertainty of the oxygen measurement is a problem. Therefore, the USP describes only the reference method but not the result of the degassing in numerical figures of the residual oxygen. Some of the persons in the dissolution lab have reported that the USP method results with approx. 1 to 2 ppm residual oxygen in the media. But this result is measured in the container of degassing and not in the dissolution test vessel. The DissoPrep delivers media with the measured results of degassing directly into the test vessel, preventing re-aeration while handling the media from bulk storage to the test vessel.

Vacuum and temperature are the most effective parameters while “additional degassing time” does not affect reasonable better results.

The edge conditions are there

a) Boiling hot water or

b) Water under absolute vacuum.

In both cases no air can be dissolved in the liquid. Our test no. 4 was performed with relative high temperature of 41°C and poor vacuum of 428 mbar while test no. 9 was performed under low temperature of 21°C and higher vacuum of 197 mbar. Both methods resulted in almost the same degassing efficiency of 5,7 to 6,1 ppm oxygen.

The combination of higher temperature and higher vacuum of the tests no. 14 and 15 resulted in reasonable good degassing efficiency of 3,1 and 2,8 ppm oxygen in the test vessel.

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In routine application of the DissoPrep the best time saving method (like test no. 10, 11, 14 and 15) delivers the most effective degassing result of 3,7 down to 2,8 ppm oxygen.

4 Conclusion

The USP reference method and other degassing methods, e.g. with helium, do not provide in routine lower degassing results in the dissolution test vessels as the DissoPrep does it .

The residual oxygen in the media is

- according the USP method: 1- 2 ppm in the container of degassing – but not after dosing into the test vessels
- with DissoPrep: in routine application methods less than 3,7 ppm (transdermal 32°C), down to 2,8 ppm (tablet 37°C) after dosing in the test vessels.

Further features are:

- automated and therefore reproducible procedure of preparing the media
- precise metering the media directly into the dissolution test vessels
- pre-warming the media
- providing a protocol documentation of the dispensing results.

5 References

[1] United States Pharmacopeia http://www.usp.org

[2] One method of deaeration is as follows: Heat the medium, while stirring gently, to about 41°C, immediately filter under vacuum using a filter having a porosity of 0.45 µm or less, with vigorous stirring, and continue stirring under vacuum for about 5 minutes. Other validated deaeration techniques for removal of dissolved gases may be used.

[3] Terry W. Moore, <A fast efficient procedure for degassing dissolution medium>, Dissolution Technologies May/1996

[4] Jennifer B. Dressman et al, <Dissolved oxygen as a measure of de- and reaeration of aqueous media for dissolution testing>, Dissolution Technologies August/1998

[5],[6] Owen S. Degenhardt et al, <Comparison of the effectiveness of various deaeration techniques>, Dissolution Technologies August/2004

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Degassing Efficiency Investigation with DissoPrep X8

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Oxymeter from WTW OXI 330
DissoPrep X8 with Firmware 8.01

Method Parameter	Test No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
Temperature set.	°C	20	32	37	42	20	32	37	42	20	32	37	42	20	32	37	42	37	37
Temperature eff.	°C/10	154	325	365	410	205	324	366	410	212	323	365	408	206	322	369	408	367	366
min. Pressure (vacuum)	mbar	489	490	484	428	269	295	274	268	197	190	193	197	98	99	99	100	99	98
Volume	mL	1x 5400	1x 5400	1x 5400	1x 5400	1x 5400	1x 5400	1x 5400	1x 5400	1x 5400	1x 5400	1x 5400	1x 5400	1x 5400	1x 5400	1x 5400	1x 5400	1x 5400	1x 5400
add. Degas Time	sec	120	120	120	120	120	120	120	120	120	120	120	120	120	120	120	120	240	480
start Oxygen	ppm O_2	9,1	8,3	8,1	9,2	8,4	8,4	8,9	8,9	8,6	8,1	8,5	8,2	8,6	8,2	8,4	8,4	8,6	8,5
end Oxygen	ppm O_2	8,2	6,7	5,9	5,7	6,5	4,7	4,7	3,8	6,1	3,7	3,4	3,3	4,6	3,1	2,8	2,0	2,7	2,7
DPX8 routine application															YES	YES