Qualification of a mixer: how to obtain the homogeneity of a mixture of powders?

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INTRODUCTION

In order to limit the development of the musculoskeletal disorders that pharmaceutical assistants (PA) develop, the pharmacy obtained funding for a mixer for the mixture of powders for capsules. The goal is to qualify the mixer by obtaining homogeneous mixtures.

METHOD

Targeted molecules and dosages:

-melatonin 1mg et 3mg
-propranolol 1mg, 2mg, 5mg et 10mg
-hydrocortisone 1mg et 2mg
-dexamethasone 2mg et 5mg
-carvédilol 1mg
-amiodarone 10mg
-spironolactone 10mg

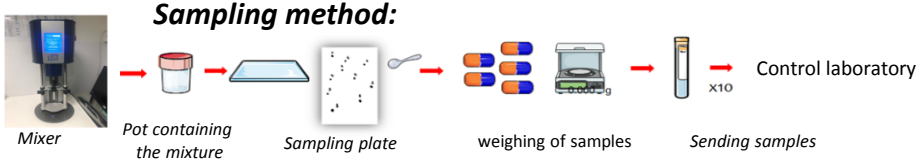
Chosen excipient:

Micronized lactose

Determined mixing parameters by an empirical method based on:

-literature
-exchanges with Hospitals using this mixer

Sampling method:



*Calculation of the CV * of the means of the content between the ten samples*

The homogeneity is proven for a CV≤5

*CV: the coefficient of variation

RESULTS

➢ **Capsule qualification test results with the new blender**

Content	MELATONIN*		PROPRANOLOL				HYDROCORTISONE*		DEXAMETHASONE		CARVEDI-LOL	AMIODA-RONE	SPIRONO-LACTONE
	1mg*	3mg*	1mg*	2mg	5mg	10mg	1mg*	2mg*	2mg	5mg	1mg	10mg	10mg
Mean of means (mg)	5,386	17,016	5,872	11,396	29,765	58,01	6,257	13,328	11,59	29,356	6,131	60,811	66,159
Standard deviation of means (mg)	0,229	0,427	0,585	0,586	1,023	2,278	0,154	0,23	0,140	0,784	0,202	1,849	0,969
CV of means (%)	4,2	2,5	10	5	3,4	3,9	2,46	1,73	1,21	2,67	3,29	3,04	1,46
Accuracy (%)	0,4	3,17	6,99	4,3	4,48	1,34	0,27	0,59	-5,23	-8,26	-3,75	-2,83	-6,71

*5% increase in active principle

Mixing parameters of the tests opposite

-mixing time: 8min
-mixing speed: 500rpm

Method bias:

-preparation environment (humidity and temperature)
-change of operators between the tests
-transport to the control laboratory

CONCLUSION

Most of powder mixtures are in accordance with the content according to the European Pharmacopoeia with demonstrated homogeneity after 8 min at 500 rpm. The influence of the mixing speed on the homogeneity is under evaluation. The PA are very satisfied with the mixer: time saving, smoother production and less repetitive movements. In addition, our establishment is a large consumer of capsules, a galenic form not always suitable for pediatrics. The results of the stability study of an oral suspension (OS) of spironolactone potentially harmful excipient with an undesirable effect were very conclusive; tests will be carried out with the mixer on the development of OS from the active principle tested previously.