TRANSFER OF TECHNOLOGY FOR PRODUCTION OF VITAMIN C tbl 500 mg

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Abstract

Vitamin C tbl 500 mg are produced by Jaka 80 AD Radovis. Due to the transfer of the production from Radovis to Skopje, there should be made a validation of the existing technology. It is made validation protocol that provides critical points in the technological process, the type of validation and the number of batches that are subject to the validation. The critical points were samples that underwent analysis of all parameters.

Key words: vitamin C, transfer technology, tablets

Introduction

Vitamin C is a vitamin that is soluble in water that is found in fruits and vegetables. It is a strong antioxidant that participates in many biological processes [1-2]. Because of the enormous importance to us we need to enter this vitamin every day in certain quantities [3-4]. If not enough is introduced through the fruits and vegetables it can be entered through the tablets, because vitamin C is first synthesized vitamin. AD Jaka 80 Radovis produces Vitamin C 500 mg tablets in which active substance is ascorbic acid. These tablets are manufactured for many years at Marshal Tito 42 in Radovis, with proven quality and standard [5-6]. Due to the commercial reasons these tablets will be no longer produced in the old location, but on the new location in a production plant at Prvomajska bb Skopje. Quality control will be done in the old location, in Quality control and testing of drugs, Skopje, Ankara, 33. Starting raw materials are from the same manufacturer with the same quality. Quantitative composition of a formulation is according to manufacturing protocol and there are no changes. Production equipment suffers slight variations due to change in a lot of quantity, but they do not cause changes in the technological production processes. Transfer of technology is made according to the requirements prescribed in this regulation [7].

Due to the change of location of production and change of the lot there is a request for approval to release the product on the market according to Commission Regulation (EC) No 726/2004, Directives 2001/83/EC and 2001/82/ec, guidelines for notice of variation of Regulations (EC) No 1085/2003 and Council Regulations (EEC) No.2309/93. In accordance with current regulations filed requests for variation Tip IB number and variation 7c Tip IA No.32b [8]. For that purpose were made two pilot series of Vitamin C tbl 500 mg a new location. He was made a comparison of all parameters of the manufacturing protocol (appearance, weight, size, strength, friability, decomposition and content). Also according validation protocols were collected and analyzed samples from several critical points production process. I needed to prove the identity of the tablets of the two locations.

Experimental part

Apparatus

The production of Vitamin C tbl 500 mg using the following equipment:

- Vibrating sieve,
- Rotating sieve,
- Powder-blender, V - blender,
- Ronchi tableting machine enclosure 23 with 7 mm matrices for tableting with broken line on one side and
- Machine for packaging in blister-packing contact AL / PVC foil.

Quality control of tablets was made with the following equipment:

- VAN KEL VK 200 tablet hardness tester - apparatus for determining the strength of tablets.
- VAN KEL friability tester - apparatus for determining friability the tablets.
- VAN KEL HAAKE DC - apparatus for the decomposition of tablets.

Procedure

To transfer technology, has been made validation protocol validation scheme. Were identified critical points in the technological process by which samples are taken for analysis (Fig 1).

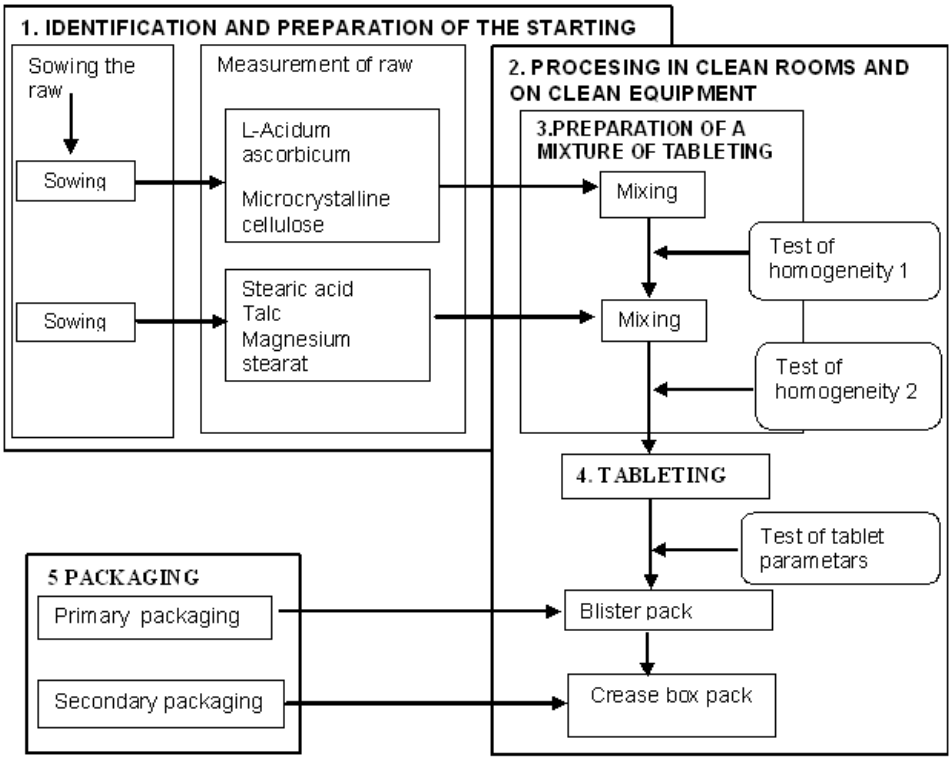

Fig.1. Validation pattern of critical parameters in the technological process

Critical points are determined after mixing the components of these tablets (including ascorbic acid), after mixing all the ingredients of these pills and after tableting. When taking a sample of granules or non tableted mixture it is taken from the mixture of three places: area middle and bottom.

Determining the content of ascorbic acid in Vitamin C tbl 500 mg is done by titration [6]. Analyzed samples from two pilot series of the new location and compared with a series of old location.

Besides changing the location change is made in the size of the lot, the existing 100 kg to 50 kg. Because of these changes the production equipment is undergoing minor changes in Phase 1 and Phase 2, which do not affect the technological procedure because tableting machine and packing machine remain the same (Table 1).

Table 1. Production equipment at both locations

Production equipment in phases	Series produced in Jaka 80 AD Radoviš-Skopje	Series produced in Jaka 80 AD Radoviš-Radoviš
Phase I	Vibrating sieve	Rotating sieve
Phase II	Powder-blender	V-blender
Phase III	Ronchi 23 tableting machine with 13 mm matrices for tableting with a break line on one side	Ronchi 23 tableting machine with 13 mm matrices for tableting with a break line on one side
Phase IV	Machine for packaging in contact packaging -blister AL/PVC foil	Machine for packaging in contact packaging -blister AL/PVC foil

Results and discussion

To make a comparison of all analyzed parameters are made two pilot series on the new location in the production plant of "Jaka 80 AD Radovis" ul.Prvomajska bb Skopje. According to protocol validation samples taken from three critical points. Taking a sample is performed by quality control. Samples from the first and second critical point are taken after the specified period of mixing (30 minutes for the first critical point and after 5 minutes for the second critical point). A sample is taken from three places on container production: surface, middle and bottom. The results of the examination of granules from first critical point are given in Table 2.

Table 2 Test of homogeneity of the first critical point

				pilot series / date	
		Given parameter	Place of sampling	01-039 05.2007	02-039 05.2007
Critical parameter	Mixing duration (min)	30 min.	Department of solid forms	30	30
Point of validation testing	Homogeneity of the mixture (mg)	450-550 mg/680 mg granules	surface	502.14	522.21
			middle	512.47	518.87

			bottom	514.35	505.69

From these results it is seen that in samples taken at the critical point 1 (by mixing ascorbic acid and some of the parts of the components) has sufficient homogeneity in samples from three different sites of the two pilot series. Ascorbic acid in all samples analyzed is within the prescribed concentration.

The results of analysis of samples from the second critical point (after mixing the components) are given in Table 3.

Table 3. Test of homogeneity of the second critical point

				pilot series / date	
		Given parameter	Place of sampling	01-039 05.2007	02-039 05.2007
Critical parameter	Mixing duration(min)	5 min.	Department of solid forms	5	5
Point of validation testing	Homogeneity of the mixture (mg)	450 -550 mg/680 mg granules	surface	505.67	513.64
			middle	504.21	519.41
			bottom	506.97	515.74

Table 4. Test of tablet parameters of the third critical point

					pilot series / data	
			Given parameter	Borders	01-039 05.2007	02-039 05.2007
Critical parameter	Speed machine(tbl/h)		-	-	30 000	30 000
	Initial pressure (kP)		(are controlled by strength)	-	2	2
	Pressure (kP)		(are controlled by strength)	-	10	10
Point of validation test	Appearance		white tablets with a flat surface, with embended line on the one side	white tablets with a flat surface, with embended line on the one side	match	match
	Average mass of tablets (mg)		680	Allowed variation ± 5.0%	680.3	680.4
	Diameter (mm)		13	13	13	13
	Strength (kp)		7.5 - 13	7.5 - 13	8.45	9.02
	Friability (%)		max 1	max 1	< 0,1	< 0,1
	Decomposition (min)		max 30	max 30	9	9
	Identification		Ascorbic acid	Ascorbic acid	match	match
	Content	mg	450-550	450-550	490.77	491.67
		%	90 - 110	90 - 110	98,15	98,33

	Total time of tableting (h)	-	-	3	3

These results also show homogeneity of ascorbic acid and its concentration in the prescribed limits.

The third critical point is after tableting, so here are taken tablets from the two pilot series immediately after the tableting. There is a determination of all parameters of the tablet. The results in Table 4 show matching values for all parameters analyzed in the two pilot series.

Conclusion

It is made a technology transfer of Vitamin C tbl 500 mg from one location to another location. Besides changing the location is changed and the lot size from 100 kg to 50 kg. To this end was made validation protocol under which samples are taken from the three critical points of the technological process. The first critical point is after the interference of ascorbic acid with some of components, the second mixing of all components and third after tableting. There have been two pilot batches of the new location. There is a determination of the content and homogeneity of the samples from the first and second critical point and determination of all parameters for the tablet samples from the third critical point. In all samples of the three critical points is observed deviation from the prescribed values. The results confirm the transfer of technology.

Literature

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