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STUDY OF THE REUSE OF CAPSULE CUTOUTS AND REPROVED CAPSULES AS RAW MATERIAL IN THE PRODUCTION PROCESS OF HARD GELATIN CAPSULES

ESTUDO DO REUTILIZAÇÃO DE RECORTES DE CÁPSULAS E CÁPSULAS REPARADAS COMO MATÉRIA-PRIMA NO PROCESSO DE PRODUÇÃO DE CÁPSULAS DE GELATINA DURA

ESTUDIO DE LA REUTILIZACIÓN DE RECORTES DE CÁPSULAS Y CÁPSULAS REPARADAS COMO MATERIA PRIMA EN EL PROCESO DE PRODUCCIÓN DE CÁPSULAS DE GELATINA DURA

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ABSTRACT

Inside of pharmaceutical industries there is a complex tangled of process and systems that always try to work the best way to improve their results, permitting the expansion of their activities and rise of their outputs. Empty hard gelatin capsules are marketed as a pharmaceutical ingredient to be filled with many kinds of medicines and have great relevancy to the product commercialized to the patient. Manufacturers of this pharmaceutical input are part of one of the bases of the world supply chain of products for drug manufacture and that's why it is important that it´s procedures are capable of keep up their customer necessities. The objective of this paper is to develop and apply methodologies to reuse side products and therefore reduce costs with raw material and by using quality control and stability studies guarantee the safety of the developed methods. In this study were developed three specific methodologies to make the reuse of capsule cutouts, full colored and colorless capsules possible. Each methodology was tested in small and large scale, with all the products of this study being analyzed by quality control areas. The study has shown that it is possible to apply

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reuse methodologies on side products, avoiding the annual discard of tons of materials and consequently reducing fabrication costs. Concluding that it is possible to conciliate industrial process optimization and cost reduction with good manufacturing procedures.

Keywords: Hard Gelatin Capsule. Reuse. Pharmaceutical Input. Rational Use of Raw Material.

RESUMO

Dentro das indústrias farmacêuticas, existe um complexo emaranhado de processos e sistemas que buscam sempre trabalhar da melhor forma para aprimorar seus resultados, permitindo a expansão de suas atividades e o aumento de sua produtividade. Cápsulas vazias de gelatina dura são comercializadas como insumo farmacêutico para o envase de diversos tipos de medicamentos e possuem grande relevância para o produto comercializado ao paciente. Os fabricantes desse insumo farmacêutico fazem parte de uma das bases da cadeia de suprimentos mundial de produtos para a fabricação de medicamentos e, por isso, é importante que seus procedimentos sejam capazes de atender às necessidades de seus clientes. O objetivo deste trabalho é desenvolver e aplicar metodologias para reutilizar subprodutos e, assim, reduzir custos com matéria-prima e, por meio de estudos de controle de qualidade e estabilidade, garantir a segurança dos métodos desenvolvidos. Neste estudo, foram desenvolvidas três metodologias específicas para possibilitar a reutilização de recortes de cápsulas, cápsulas coloridas e incolores. Cada metodologia foi testada em pequena e grande escala, com todos os produtos deste estudo sendo analisados pelas áreas de controle de qualidade. O estudo demonstrou que é possível aplicar metodologias de reuso em subprodutos, evitando o descarte anual de toneladas de materiais e, consequentemente, reduzindo os custos de fabricação. Conclui-se que é possível conciliar a otimização de processos industriais e a redução de custos com bons procedimentos de fabricação.

Palavras-chave: Cápsula Gelatinosa Dura. Reaproveitamento. Insumo. Farmacêutico. Uso Racional de Matéria Prima.

RESUMEN

Dentro de la industria farmacéutica, existe una compleja red de procesos y sistemas que buscan constantemente mejorar sus resultados, lo que permite la expansión de sus actividades y el aumento de la productividad. Las cápsulas de gelatina dura vacías se venden como ingrediente farmacéutico para el envasado de diversos tipos de medicamentos y son de gran importancia para el producto que se vende a los pacientes. Los fabricantes de este ingrediente farmacéutico forman parte de uno de los pilares de la cadena de suministro global de productos farmacéuticos, por lo que es crucial que sus procedimientos satisfagan las necesidades de sus clientes. El objetivo de este trabajo es desarrollar y aplicar metodologías para la reutilización de subproductos y, así, reducir los costos de las materias primas y, mediante estudios de control de calidad y estabilidad, garantizar la seguridad de los métodos desarrollados. En este estudio, se desarrollaron tres metodologías específicas para permitir la reutilización de recortes de cápsulas, cápsulas coloreadas y cápsulas incoloras. Cada metodología se probó a pequeña y gran escala, y todos los productos del estudio fueron analizados por los departamentos de control de calidad. El estudio demostró que es posible aplicar metodologías de reutilización a los subproductos, evitando el desecho anual de toneladas de materiales y, en consecuencia, reduciendo los costos de fabricación. La

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conclusión es que es posible combinar la optimización de procesos industriales y la reducción de costes con buenos procedimientos de fabricación.

Palabras clave: Cápsula de Gelatina Dura. Reutilización. Insumos Farmacéuticos. Uso Racional de la Materia Prima.

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1 INTRODUCTION

The constant rise of the world demand for pharmaceutical inputs makes the necessity for these items grow in a directly proportional way, forcing companies to always seek new strategies for making good use of the available resources. The benefits brought by this mentality headed on continuous improvement goes from cost reduction with raw material and unnecessary wasting to the constant influx of material for production usage (Santo, 2021).

For this reason, scientific research headed towards optimization of industrial processes always try to be updated along with time, bringing new technologies and procedures to reach the best results on quality, shipping time and final cost (Carvalho, 2010).

The productive process of empty hard gelatine capsules is based on manipulating an animal or plant-based gelatine solution that is subsequently used to mould the capsules in specific equipment known as hard capsule making machine (HCMs). In these machines the gelatine solution is kept in storage tanks that feed the moulding process happening in stainless steel pins installed on the machine. These pins are the moulds of the caps and bodies of capsules which will subsequently be trimmed and jointed by mechanisms of the HCMs itself generating the main product and the capsule cut-outs that are a by-product of the process. This process depends on many physical and chemical parameters that must be accurately followed to reduce imperfections on the product that has been moulded (Lachman et al., 2001).

Physical imperfections, when not avoided during production phase, are listed, recorded and segregated, ensuring that the best quality capsules are delivered to the customer. In addition to the reproved capsules, the mechanisms of HCMs itself create a great amount of gelatine trims, that are the cut-outs of the exceeding amount of gelatine solution stuck on the pins. All this reproved and segregated material represents considerable loss of raw material, labour and production time., it is plausible to study ways to avoid these reproves or reuse the segregated material (Lachman et al., 2001).

One of the greatest recent technological advances is the automating of the inspection process of the capsules, which was initially done manually, by work of many human sorters in a slow and exhausting process. Today it counts on equipment capable of automating the process with much more efficiency and accuracy. The company Eli Lilli & Comp. has patented an electronic equipment that has a sorting mechanism that can evaluate the capsules by optical sensors that can detects imperfections and segregate them automatically from the finished product (lachman et al., 2001).

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The practice of reusing residuals and by-products has been used and implemented in other industries for a while now, for example, the food and nutraceutical industries are used to apply this kind of knowledge avoiding the discard of tons of organic residuals annually. By-products of food industries are being used on development of functional flours based on parts of fruit as blueberry juice processing residuals and residuals of processing of olive oil. In nutraceutical industries the gelatine capsules and chia oil are used as base for making biodegradable packages (Crizel, 2017).

The objective of this project is to reduce the discard of pharmaceutical by-products by developing and applying methodologies to make possible the reuse of these by-products on the production process. The capsules selected for reuse ware reproved and segregated on the sorting phase for presenting physical imperfections that prevented its commercialization. When capsules can't be sold, they must be grinded and sent to incineration or be sold to less important uses, representing great material loss and additional cost. It was developed, applied, and evaluated three methodologies to enable the reuse of capsule cut-outs, full colourless and coloured capsules, and separated capsules. At the end of this study ware ran physic-chemical and microbiological tests as well as stability tests on batches produced with 65%, 80%, and 100% of reused material content to guarantee the safety of the methodologies described on this paper.

2 METHODOLOGY

2.1 SMALL SCALE APPLICATION

In a laboratory bench, after theoretical planning of all steps of the study, were developed ways to replicate, in small scale, the process of, molding and drying of the gelatin solution, to permit the validation of the study before applying it in industrial scale.

To prepare the colorless and colored gelatin solutions, the titanium dioxide suspension, that was added to the process as an opacifier, and to mold the flat gelatin films were used the following equipment's: Water bath model NT245 made by Novatécnica, Analytical balance model AR2140 Toledo brand, Mechanical stirrer model 713D Fisaton brand, immersion mixer model PMX900PI Philco brand, Beckers made out of glass and polypropylene, polypropylene test tubes and laboratory spatulas made on acrylic or stainless steel. To measure the properties of the solutions, suspensions, flat films, and capsules was used: Rotational viscometer, moisture analyzer Mettler Toledo brand model HX204, digital

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pachymeter and dial indicator both Mitutoyo brand, digital thermometer and some equipment's developed in house.

First, in a two-litter Becker made from polypropylene, was diluted under constant mixing, in a two to one proportion, enough amount of gelatine granules in purified water (P.W.), heated to 60ºC until it forms a homogeny viscous solution. In this solution were added all the inputs needed to the industrial scale production, which was, as well as the gelatine granules, measured in a Becker with an analytical balance. After prepared, this solution was kept in a water bath for four hours while, periodically, was sampled for evaluation of its viscosity, appearance and moisture using the previously mentioned equipment's.

As the properties kept stable during the resting period in water bath, the gelatin solution was used to mold a flat film using two molds made of acrylic and stainless steel that work together to create a film with thickness close to a capsule wall. The molded films were then transported to the drying chambers where they stayed for 45 minutes, enough time to reduce its water content from 70% to 14,5% (the results ranged between 13% to 16%). they were than named and coded before being stored to, when needed, be consulted for evaluation.

On next phase, the following byproducts were selected to keep on the study: gelatin cutouts, colorless and colored capsules segregated on electronic sorting for having physical imperfections and joined capsules with formulation of body and cap different from each other also reproved for having physical imperfections.

Based on the byproducts previously selected, was applied a reverse math based on what was seen on the drying process to determine the quantitative of each input present in the material destined for reuse and final concentration of each input after diluting the material in two parts of hot purified water.

Were weighted, on an analytical balance, 300 grams of gelatin cutouts, colorless capsules, colored capsules with formulation of cap and body different and equal from each other and at last, caps and bodies previously separated from each other. This material was then dissolved in purified water, at 60ºC, using the two to one proportion under constant mixing until it forms a viscous homogeny solution. As the quantitative of each input present on this solution was known, it was possible to subtract it from the formulation of different products intended to be manipulated, ending the process by adding the rest of the material needed to obtain the desired formulation. This way it was possible to manipulate in small scale many products previously developed.

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Just as it was done in the first practical part of the study, all manipulated solutions were kept in water bath for four hours, where they were periodically verified to see any possible oscillation on its viscosity, appearance and humidity. At the end of the resting period, the gelatin solution was used to make the flat films by using acrylic and stainless-steel molds. Making these flat gelatin films is important to replicate in small scale the molding and drying processes that happen on the HCMs.

The films had their appearance, color and humidity properties analyzed with naked eye and by using a moisture analyzer. The results were then compared to the results obtained from films produced without using reprocessed material and capsules with the same quantitative and qualitative formulation, molded on HCMs and destined to be sold.

2.2 INDUSTRAL SCALE REPLICATION:

For this part, along the previously mentioned equipment, were used equipment's, tools and utensils destined for industrial scale production as reactors, industrial mixers, stainless steel tanks, digital balance Toledo brand, semi-analytical balance Toledo brand model ARD110, heating systems, HCMs, electronic sorters and other equipment developed in house.

Initially, after all math is done, were selected many samples of each interest material for this study. While being produced, the batches which were selected to be posteriorly reused, were closely followed to be sure that nothing was being done out of what was intended. As each product has its own formulation, were used many samples with formulations previously selected, that has segregated from 10kg to 50kg of material each.

After quantitative and qualitative evaluation of each formulation, in an area designated for manipulation, were dissolved, in a two to one proportion of purified water and material for reprocess respectively, in stainless steel tanks, enough amount of each sample to produce gelatin solutions with a 65%, 80% and 100% amount of material to be reprocessed. The time needed to dissolve all this material ranged from 30 minutes for cutouts to 02h30min to non-separated capsules.

The manipulation process ended with the addition of virgin gelatin solution, opacifier, colorants and all needed inputs to complete 100 liters of gelatin solution, this way fulfilling the formulation of previously produced products for posterior comparison of their quality control results. The gelatin tanks were kept resting for around six hours, and their appearance, viscosity and humidity properties were periodically evaluated, just the way it was done on

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bench scale. As these properties kept stable, the tanks were transferred to the production area, where they were used to feed the molding process on the capsule making machines (HCMs).

All batches produced were labeled and segregated from the products destined to commercialization, while a small sample was sent to the microbiological and physical-chemical quality control areas. In These areas was made the following tests: The search of bacterial or fungal growth that could be present contaminating the capsules, disintegrating time test, appearance, and manual filling test, according to Brazilian legislation RDC 34 of 2015, that disposal the good manufacturing procedures for pharmaceutical inputs (ANVISA, 2015).

As all evaluated properties had their results according to the stipulated parameters, the batches were sent to accelerated and shelf-life stability study, in which on time zero and after three and six months had all its parameter re-evaluated.

3 RESULTS AND DISCUSSION

3.1 REUSE OF CAPSULE CUTOUTS:

The number of cutouts produced is directly related to the number of capsules produced and the technical specifications of the HCM making them. In this study, the machines used were industrial models capable of producing around one million capsules of uninterrupted production per day.

Each produced and evaluated capsule generated two gelatin cutouts from cap and body respectively. These cutouts represent from 40% to 50% of the full capsule weight, meaning that a batch of one million capsules weighting 97 milligrams each, have generated in average 43,650 Kilograms of material segregated in gelatin cutouts. As the weight of each capsule size is known, it was possible to determine using the following equation the amount of segregated material for each produced million capsules.

Total amount of gelatin cutouts produced = weight of the capsule * capsules produced * % of weight of two cutouts related to the full capsule

The gelatin cutouts were constantly transported using a compressed air system connected to tubes leading to a vertical stainless-steel collector where they were kept being periodically collected, making the procedure and transportation easier.

As this byproduct was posteriorly used to manipulate new batches, GMP (good manufacturing procedures) were followed to guarantee the safety of the products that were

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being made. One important consideration was the keeping of the material in a quarantine zone while the microbiological tests were being ran (ANVISA, 2022).

After its safety was attested, the formulation of each product that has originated the gelatin cutouts was evaluated to determine the amount of raw material present in each kilogram of material for reprocess.

To understand the way the quantitative of each material for reprocess is calculated, it is first necessary to understand the methodology used to quantify the composition of each capsule. So, this way, it is necessary to understand the relation between each input's concentration in one liter of gelatin and the amount, in milligrams, of each input present on the finished capsule (g/l = mg/capsule).

The conceptual base developed for the theoretical calculation started with the exact quantitative survey of all components present in the gelatin solution. They were Animal gelatin, water, colorants, and other inputs needed to large scale production. The weight of all inputs added was noted and converted to its respective percentage against the total weight of the gelatin solution. This way it was defined the distribution of the weight of the components present on the gelatin solution.

The second step made was the evaluation of all parameters of finished products, permitting this way to rationalize the physical-chemical processes that was happening in the drying phase. The humidity was measured using moisture analyzer equipment, in which the capsules that had its water content ranging from 13% to 16% were approved non-depending on its size. For theoretical calculation was considered the average of 14,5% for the water content present on the finished product.

The diluting of the gelatin granules was made using purified water heated to a temperature between 55ºC to 65ºC in two parts of water to one part of gelatin proportion. The physical-chemical properties of the animal-based gelatin permit that when heated to temperatures above 37ºC in aqueous ambient it transforms in a concentrated viscous solution, which is the intermediate product that feeds the molding process (Duconseille et al., 2014).

With the goal of putting colors on the capsules were selected the following colorants: Quinoline yellow, brilliant blue, allura red, carmoisine and sunset yellow that were dissolved in purified water in a proportion of 35 milliliters for each colorant gram. The titanium dioxide was used as an opacifier in form of a stable suspension because it is chemically insoluble in

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water. Just as the colorants, the titanium dioxide was incorporated after the process of manipulation of the colorless gelatin solution was done.

Because of its known pharmacotechnical and pharmacological importance, the organoleptic characteristics of the finished product were carefully defined on the development processes. It is common that patients, either by themselves or by indication of some health professional, use

the organoleptic properties of medicines as a way of identifying them. This kind of strategical approach happens mainly in elderly patients going through treatments that require them to consume great variety of medicines or unlettered people (Bechi, 2015), (Barbosa; Polita; Monino, 2008).

The third and last step to finish the theoretical calculations was done by comparing the water content on the gelatin solution and the finished capsule to measure the total mass reduction. The drying process happened in the stainless-steel pins of the HCM in a process that take around 45 minutes to complete and uses mechanisms of the HCM itself. After evaluation of the physical-chemical properties of each input present on the formulation of the gelatin solution was possible to conclude that none of the components except the water, is volatile in the temperature of the drying chambers, which is 25ºC. As the only source of mass reduction was identified to be water, it was possible to redistribute the weight percentage of each input and calculate the values in milligrams of material per capsule produced. Considering the water present in the gelatin granules, the initial content of water was 70% averaging plus or minus 5%, and the content of water in the capsule ends up in 14,5% averaging plus or minus 1,5%, both results obtained by the loss on drying method. This reduction on the water content corresponds to a loss of 55% of the initial weight. Resuming, for each 1 kg of gelatin solution were produced around 550g of

capsules and gelatin cutouts, meaning that as each capsule generate in average 45% of its own weight in cutouts, the effective weight produced is 302,5g of capsules and 247,5g in cutouts segregate by the HCM. Table 01 considers how much one kilogram of gelatin will produce in capsules and gelatin cutouts, on the main produced capsules sizes.

Considering table 01 and a production of one million capsules for HCM we could calculate that the benefit brought by this methodology is the reuse of 13,0kg to 54,33kg of material for each machine depending on the size that is being produced.

The process of diluting the gelatin cutouts was made using manipulation tanks, made of stainless steel, that can hold 150 liters of gelatin each, and industrial mechanical mixers

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responsible for keeping the solution always in motion during this part of the process. As the capsule cutouts have great contact area with the solvent, in this case water, it was possible to dissolve all material enough to make a 100% reused tank within 30 minutes.

Table 1

Average yield of 1kg of gelatin solution

Size	Average weight (mg)	Capsules produced	Segregated in cutouts (kg)
000	163	1.855,83	0,2475
00	119	2.542,02	0,2475
0	97	3.118,56	0,2475
1	76	3.980,26	0,2475
2	61	4.959,02	0,2475
3	48	6.302,08	0,2475
4	39	7.756,41	0,2475

Source: Table by the authors themselves.

3.1 REUSE OF COLORLESS AND COLORED CAPSULES

As it was mentioned on introduction, because of the complexity and the needing of many parameter adjustments in machinery and intermediary products, it is not always possible to guarantee the approbation of all capsules produced. So, the main idea behind this methodology is to reduce the Impact caused by unperfect non-sellable capsules produced along the batch. Because of the capability of the electronic sorting on identifying and automatically segregating the unperfect capsules it was very plausible to apply the following technics.

The benefit brought by applying this methodology, in this case, is directly proportional to the number of discarded capsules because of physical defects. It means that the more reproved capsules, the more capsules will be available to be reused. Considering a production of a million capsules with an approval rate of 95%, and the 5% remaining being reproved for presenting physical defects it is possible to see on table 02 the amount of segregated material.

The same way it was done with the gelatin cutouts, the capsules destined for reuse using this methodology was kept on quarantine while being evaluated by the microbiological quality control area. When they were approved, because of it being a finished product, its

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quantitative and qualitative formulation was already known, turning the math to be just a multiplication of the composition of one capsule for the weight available to reprocess.

Capsules, without being previously separated need more time to be dissolved because of its lower contact area with the solvent. It took around 2h30min to dissolve, under constant mixing, each tank made of 100% capsules for reprocess. Although it needs more time on the manipulating process this is not a condition that avoids it to be done.

Table 2

Amount of material segregated in reproved capsules (approval rate of 95%)

Size	Average weight (mg)	Segregated capsules	Material avaliable for reuse (Kg)
000	163	50.000	8,15
00	119	50.000	5,95
0	97	50.000	4,85
1	76	50.000	3,80
2	61	50.000	3,05
3	48	50.000	2,40
4	39	50.000	1,95

Source: Table by the authors themselves.

3.2 REUSE OF CAPSULES THAT HAS ITS FORMULATION OF CAP DISTINCT FROM ITS BODY

In the case of capsules with two different colors it is common that the number of colorants in its formulation rise. That is because different colors require different quantitative and qualitative combinations to be manipulated. This rise in complexity turned the methodology to be more difficult because the possibility of reuse or not it is, beyond other factors, related to the formulation of the developed product that it's intended to produce and that it is supposed to receive the material to be reprocessed.

Were applied two different ways to overcome this raise in complexity, the first one, is simpler, consists in calculating theoretically the inputs present on the cap and on the body of the capsule, defining the weight distribution of body and capsule before applying the calculations to find the number of present inputs. After this math is done the quantitative formulation of the full capsule will be known, permitting to reuse it as it is. The second explored way required an in house developed equipment, which is goal is to separate the cap

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from the body of the capsule. As the formulation of the parts is distinct, separating them becomes easier to find compatibility to other developed product.

The benefit brought by applying this methodology is also dependent on the approval rate on the production phase, meaning that the lower the percentage of approved capsules the higher will be the number of capsules available for reprocess. Talking about products in which was seeing the impossibility of reuse because of incompatibility to other products was added the separation phase to the process. This way it is also possible to consider table 02 to exemplify the benefit brought by this methodology.

3.3 QUALITY CONTROL AND STABILITY STUDY

With the goal of guarantee a representative result, all boxes produced was sampled during and after production phase. The samples generated were labeled and sent to physical-chemical and microbiological evaluation.

At the end of the production campaign all batches produced with 65%, 80% and 100% of reused material were sent to accelerated stability tests and shelf-life stability tests, where it was done the evaluation of all properties of finished products on initial timing, after three months and after six months. On every analysis, were taken samples of three colored and three colorless batches, making the study to become more statistically robust.

As it can be observed on the annexes, the results named as ACR65% and ACL65% represent the average of the tests ran on three colored and three colorless batches produced using 65% of reused material respectively. Following the same thinking line, we find the test results named as ACR80% and ACL80% representing the average of the results of three colored and three colorless batches produced using 80% of reused material respectively. At the end there is the average results of the tests ran on three colored and three colorless batches produced using 100% of reused material. The average results are named as ACR100% and ACL100% respectively.

On the shelf-life stability study the batches were kept on climate chambers in ideal storing conditions, with its temperature maintained within the limits of 15ºC to 25Cº and humidity from 35% R.H. to 65% R.H. and never being exposed directly to light. The accelerated stability test puts the capsules propositionally in stress conditions, with the goal of evaluating how they will react. The storage conditions in this study rise the temperature to 35ºC, relative humidity of the air to 75% and expose the capsules directly to light. As it can be seeing on the annexes, two lines, blue and red are oscillating vertically inside of the limits

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proposed for the study. The lines show how the samples reacted to the different storing conditions, the blue line represents the capsules placed on accelerated stability study and the red line represents the perfect storing condition stability study. None of the tests kept its initial condition but, considering some variables like the equipment used and the procedure being made by different analysts the results of both conditions didn't exceed the specification limits.

First, it was evaluated the microbiological conditions of each sample by counting the total of bacterial and fungal that grow on agar. Then it was made the search of the pathogens Escherichia coli, Pseudomonas aeruginosa, Salmonella sp and Staphylococcus aureus. After the microbiological work is done, the capsules were sent to have their organoleptic properties evaluated, being them color, description and appearance. It wasn't seeing any significant change from its initial condition on the organoleptic properties.

The microbiological analysis was made by using the "Pour Plate" method that consists in adding 1ml of the diluted sample in a tamponed solution in a sterile plate, followed by instilling around 17ml of the culture medium. The mediums used were the "Sabouraud Dextrose (SDA)" for fungal growth and "Tryptic Soy (TSA)" for bacterial growth. It was not seeing any microbiological growth in any of the samples from the shelf life and accelerated stability study.

At last, the capsules were sent to physical-chemical evaluation, where it's dimensions, weight, brittleness, manual filling, torque needed to separate the cap from the body (Shimpo), excessive facility on separating the body from the cap (Venturi test), disintegration time and humidity were tested.

The following figure 01, show the average results of the humidity test made on three colored batches made of 100% of reprocessed material (ACR100%).

The humidity tests were done using twenty capsules and a moisture analysing balance, that heat the capsules to a temperature enough to evaporate all the water present in the capsules. The difference between initial and final weight must be between 13,0% to 16,0% representing the loss on drying weight.

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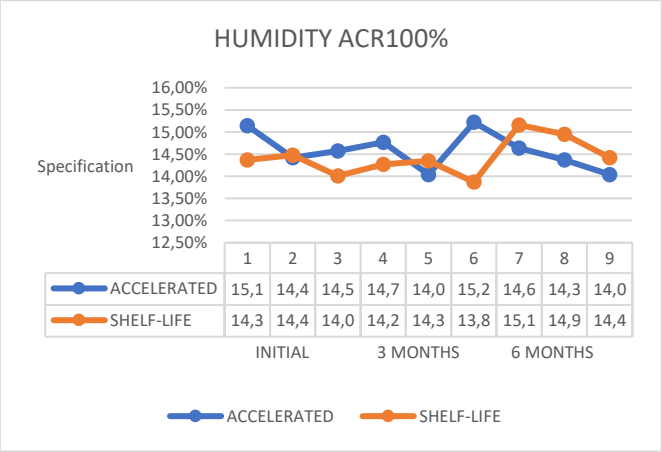
Figure 1

Average humidity content graphic on initial timing, after three months and after 6 months



Source: Graphic by the authors themselves.

Just as it was done to all other analysis on this paper, were taken three sample of each batch on every period on both storing conditions. As it was produced three batches, the results shown on “1, 2 and 3” are the average result of the tests ran on the initial timing of the three batches. The results “4, 5 and 6” represent the average result of the tests ran on the three batches sampled after three months under storage. On the end we have the results “7, 8 and 9” representing the average result of the tests ran on the three batches sampled after six months under storage. With all said it is important to highlight that the tests were ran on different days and by different analysts to guarantee the accuracy of the evaluative method applied.

4 CONCLUSION

During any productive process, one of the biggest challenges to be obtained is an efficient production counting the smallest possible number of incompatibilities to the determined parameters. However, this isn’t always possible, turning the reprocess only one of the strategies used to mitigate the negative effects generated.

As it was discussed along this paper, the application of these three developed methodologies can avoid the discard of tons of segregated material annually, reducing costs, waist of raw material and always seeking ways to make rational use of the available resources.

It is impossible to negate the products intended to be consumed by humans need more care during its production. Because of that, it is always needed to pay attention to the rules

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and regulatory statements of every material that is being used or produced. Rules and technical requirements are always available and updated by the sanitary vigilance to guarantee control and make the managing of industrial process easier. By using the presented study as an example, the making of pharmaceutical inputs brings a big systemic perspective of development and quality management.

Thinking about continuous improvement we must always propose changes with very concise goals for the company and always keeping quality and respect to the end customer in mind.

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