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PROCESS SCALE UP OF IBRUFEN TABLET

Shashank Tiwari*, Sachin Saxena, Rohit Kumar
Amity Institute of Pharmacy, Department of Pharmaceutics, Amity University, Lucknow (U.P.)

Abstract:
Scale up is generally defined as the process of increasing batch size. In process scale up a formula is transformed into a viable, robust product by the development of a reliable and practical method of manufacturing that effect the orderly transition from laboratory to routine processing in a full-scale production facility. It must include a close examination of the formula to determine its ability to withstand batch-scale and process modification. So process scale up of Ibrufen tablet includes Trial Batches, Exhibit Batches and Validation Batch. After these batches produce large scale up Ibrufen Tablets. Ibrufen is a Non-steroidal anti inflammatory drug use for relive symptoms of arthritis, fever, as an analgesic. During the scale up process controls are evaluated, valuated and finalized in addition, appropriate records and report are issued to support good manufacturing practices and to provide the historical development of the production, formulation, process equipments train, and specification.

Keywords: Scale, laboratory, validation, fever, arthritis, batches, formulation

Introduction:

Scale-up is generally defined as the process of increasing batch size. Scale-up of a process can also be viewed as a procedure for applying the same process to different output volumes. There is a subtle difference between these two definitions: batch size enlargement does not always translate into a size increase of the processing volume. In mixing applications, scale-up is indeed concerned with increasing the linear dimensions from the laboratory to the plant size. On the other hand, processes exist (e.g., tableting) where the term ‘‘scale-up’’ simply means enlarging the output by increasing the speed. To complete the picture, one should point out special procedures (especially in biotechnology) where an increase of the scale is counterproductive and ‘‘scale-down’’ is required to improve the quality of the product. In moving from research and development (R&D) to production scale, it is sometimes essential to have an intermediate batch scale. This is achieved at the so-called pilot scale, which is defined as the manufacturing of drug product by a procedure fully representative of and simulating that used for full manufacturing scale. This scale also makes it possible to produce enough products for clinical testing and to manufacture samples for marketing. However, inserting an intermediate step between R&D and production scales does not, in itself, guarantee a smooth transition. A well-defined process may generate a perfect product both in the laboratory and the pilot plant and then fail quality assurance tests in production.

Ibuprofen (ios-butyl-propanoic-phenolic acid) is a nonsterodial anti-inflammatory drug (NSAID) used for relief of symptoms of arthritis, fever, as an analgesic(Pain reliever), especially where there is an inflammatory component, and dysmenorrhea[1].

A white to off-white crystalline powder having a slight characteristic odour. Practically insoluble in water; very soluble in alcohol, in acetone, in chloroform, and in methyl alcohol; slightly soluble in ethyl acetate. Store in airtight containers[2].

Dose:

Ibuprofen has a dose-dependent duration of action of approximately four to eight hours, which is longer than suggested by its short half-life. The recommended dose varies with body mass and indication. 1,200 mg is considered the maximum daily dose for OTC use, though, under medical direction, the maximum amount of ibuprofen for adults is 800 milligrams per dose or 3200 mg per day[1].

Unlike aspirin, which breaks down in solution, ibuprofen is stable, and, thus, ibuprofen can be available in topical gel form, which is absorbed through the skin, and can be used for sports injuries, with less risk of digestive problems[1].

Empirical Formula: $C_{13}H_{18}O_2$
Formula weight: 206.12gram/mole
Appearance: White Powder
Use:- Ingredient in over the counter pain reliever
Melting Point: 77-78 ^{0}C
Enthalpy formulation:- 14114 kJ/mol

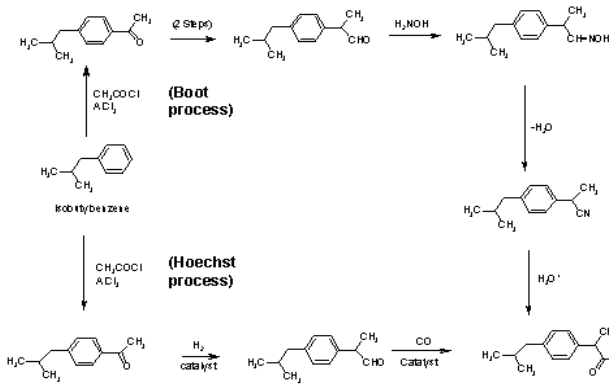
Solubility: Stable. Combustible. Incompatible with strong oxidizing agents

Storage Condition:- 20-25 ^{0}C (68-77 ^{0}F)

Disposal: Whatever cannot be saved for recovery or recycling should be managed in an appropriate and approved waste disposal facility. Processing, use or contamination of this product may change the waste management options. State and local disposal regulations may differ from federal disposal regulations. Dispose of container and unused contents in accordance with federal, state and local requirements.

Toxicology: Harmful if inhaled, swallowed or absorbed through the skin. Possible risk of irreversible effects. Possible mutagen. May cause eye and skin irritation. May cause respiratory and digestive tract irritation. May cause kidney damage.

Synthesis:



There are two ways to synthesize ibuprofen - - the Boots process and the Hoechst process. In both cases the starting material is 2-methylpropylbenzene, made from crude oil. This compound has a similar carbon skeleton to that of ibuprofen. The reagent and product are also the same in both cases. In the Boots synthesis, more than half of the materials used in the synthesis are wasted. This is because the .catalyst. used in this synthesis (aluminium trichloride, AlCl3) is not a true catalyst. It is changed into a hydrated form that cannot be reused. The catalyst in the Hoechst process (the green synthesis) is hydrogen fluoride, HF which can be recovered and reused. Two other catalysts (Raney nickel and palladium) are used in the green synthesis, which makes the method cheaper and more environmentally friendly. The compound (4-Isobutyl-a methylphenylacetic acid, 99%) can be purchased from any laboratory chemical suppliers like Alfa Aesar, in 1g, 5g, and 25g batches. The pharmaceutical form of ibuprofen can be purchased at any pharmacy, supermarkets, and convenience stores often in 200 mg tablets.

Step of Process Scale Up:

Mainly three of process scales up batches

1. Trial Batches
2. Exhibit Batches
3. Validation Batches

After validation batches we produce large scale up of Ibrufen tablets.

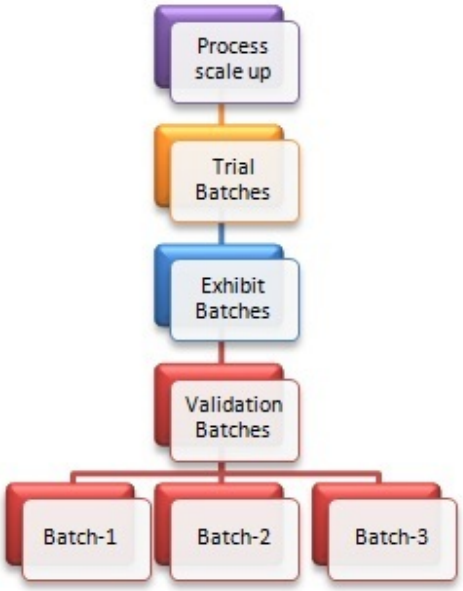
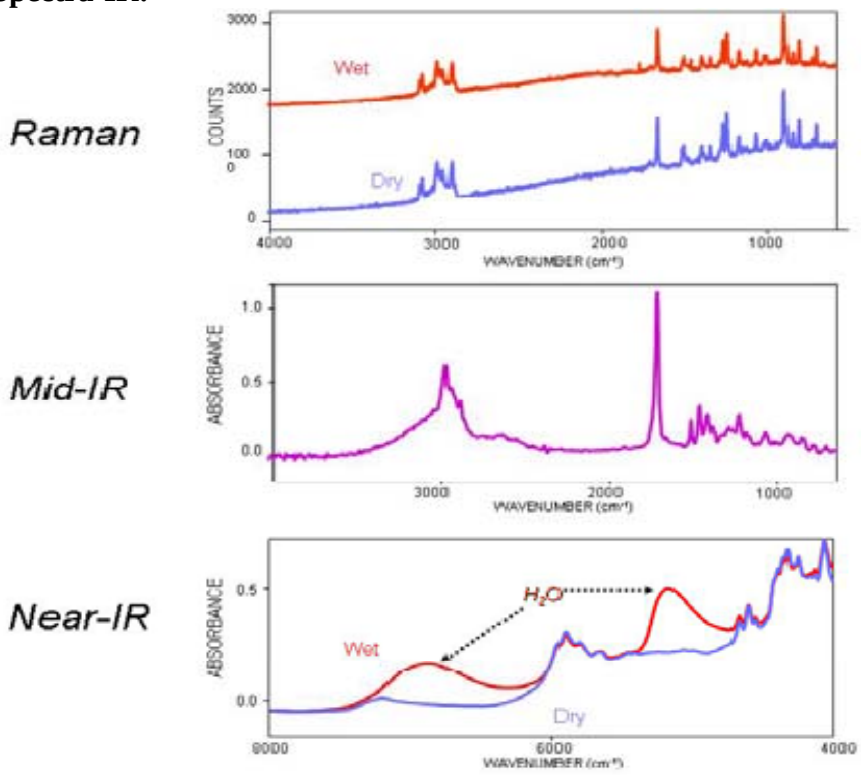


Chart which is describe step of Process Scale up of Pharmaceutical Industry

1.Trial Batch:

Trial Batches are small quantity of batch size; these batches are getting to the after R&D (Research & Development) division. The quantities of this trial batch are near about One thousand to 1 lack. In these batches we check the Stability and Dissolution and other many factors.

Spectra-IR:



UV:

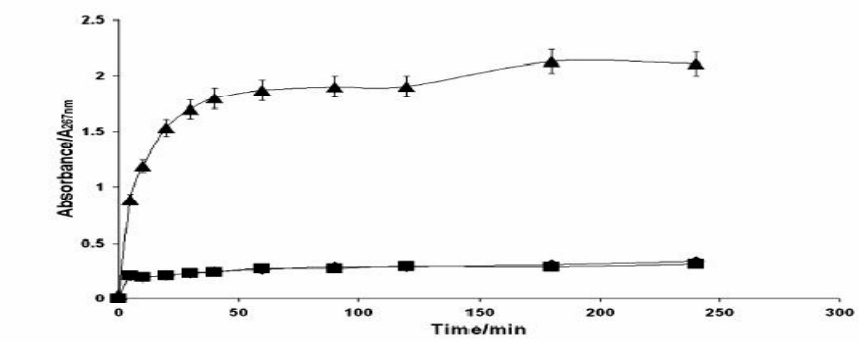
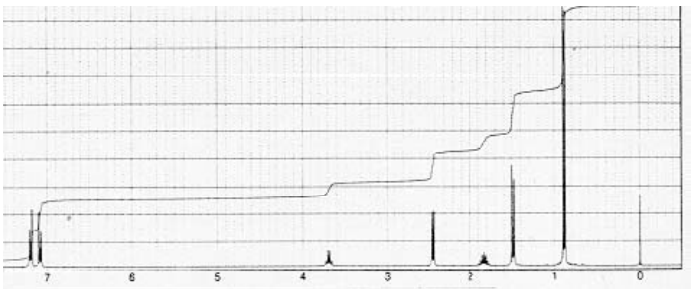


Fig. 3 UV-vis spectra showing release of ibuprofen from (▲) silica, (◆) calcium carbonate and (■) calcium phosphate replicas.

NMR:



S.No.	Country Name	Approval Body
1.	INDIA	FDA
2.	UNITED STATE	USFDA
3.	UNITED KINGDOM	MHRA
4.	BRAZIL	ANVISA
5.	TANAZINIA	TFDA
6.	UGANDA	NDA
7.	KENYA	PPB
8.	COLUMBIA	INVIMA

2.Exhibit Batch:

The main purpose of the exhibit Batches are to approval the market in which country we export the Drugs. For Example

The quantities of these batches are near about one lack to 10 lacks. The Exhibit batches is the most Important batches are the in these three process scale up batches. Its prepare to very careful and expert hands. In exhibit batches the time of duration are very long because the approval issue. These approval time near about 9 to 12 months.

3.Validation Batches:

Once the country are approved the drugs then we are started the validation batches. These batches are divided in to the three parts Batch-1, Batch-2 and Batch-3. The validation batches are the important to the process scale up techniques. Like the speed of machines is important role of the process of the manufacturing of the any drugs. We check the in these three batches and finally we take the average speed of the machines. After completion these three batches we compile the data of batch-1, 2, and 3. Then make the record book or SOP (Standard Operating Procedure) which is followed by the production department. And produce the large quantity of the drugs and then export the approved market.

Note:- Validation Batches are also export the approved market.

For manufacturing Ibrufen Tablet following 20 steps

1. Dispensing
2. Sifting
3. Dispensed Material Quantity Verification
4. Granulation
5. Drying
6. Dry Screening and milling
7. Blending
8. Quality Control check
9. Compression
10. Coating
11. Sub coating
12. Smooth Coating
13. Color coating
14. Polishing
15. Store the polishing tablet
16. Printing of tablet
17. Inspect the printing tablet
18. Store the inspect tablet
19. Finished product Analysis by QA
20. Packaging

Note- 1) Smooth Coating Solution has to be used within 72 hours of the manufacturing. Dispose of any unused or expired material immediately.

2) The wet Granulation Should be dried immediately after granulation.

For Ibrufen Tablet can make these Steps

For Example: - Batch Size- 200mg/ 304.700 kilogram- 1100000 tablets

1. Fabrication
2. Seal coat

3. Sub coat
4. Smooth coat
5. Color coat
6. Polishing
7. Tablet Printing (If Required)

Parameters: - (These parameters Only Just a Example)

1. Granulation

A. Drying Mixing Time (min)
B. Binder Addition Time (min)
C. Granulation Time (min)
D. Extra quantity of purified water add (Kg)

2. Compression

A. Discription- white, Round Shaped Tablet plain on both Side
B. Average weight- (667.0± 20 mg)
C. Uniformity of weighty- (± 8% of avg. weight)
D. Thickness- (6.0± 0.3 mm)
E. Hardness (Kp)- NLT 3 Kp
F. Friability- NMT 1.0% w/w
G. Disintegration time- NMT 20 min

3. Coating

A. Pan Speed- (6-9 rpm)

4. Sub Coat/ Smooth Coat

A. Inlet Temp.
B. Outlet Temp.
C. Pan Speed
D. Spray Rate
E. Dosing Time
F. Rolling Time
G. Drying Time

Conclusion:

The key to scaling up of an Ibrufen tableting process is to consider it during the entire development process. From the inception of a development project, the formulation scientist must consider scale-up. It should not be a process removed from development process. Scale up is a, inserting an intermediate step between R&D and production scales does not, in itself, guarantee a smooth transition. A well-defined process may generate a perfect product both in the laboratory and the pilot plant and then fail quality assurance tests in production.

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