DETAILED FEASIBILITY ANALYSIS OF DRUG FORMULATION

Part II

For

DEPARTMENT OF INDUSTRIES

MINISTRY OF ECONOMIC AFFAIRS

ROYAL GOVERNMENT OF BHUTAN

By

IDRG CONSULTANCY SERVICES

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CONTENTS

CHAPTER 1 - PROJECT AT A GLANCE

1. Project concept – Detailed feasibility analysis of **drug formulations**. The project envisages the manufacture of drug formulations mainly paracetamol, anta-acid and iron-folic acid in tablet form, vitamin B complex in capsule form and ORS in powder form. Other need based drug formulation could also be manufactured in tablet or capsule form.

2. Location - Thimphu, Phuentsholing, Paro, Punakha, Gelephu and Samdrup being the major towns have potential for a drug formulation unit. However, keeping in view that at present, almost the entire supplies of drug formulations in Bhutan are procured by the government as well as various other parameters, these locations have been short listed in the order of preference as under.

Location	**Overall rating**
Thimphu	**48**
Phuentsholing	40
Paro	37
Punakha	35
Gelephu	34
Samdrup	33

3. Markets - Majority of the drug formulations in Bhutan are procured centrally by Ministry of Health and then distributed through various hospitals in the country. There are medical stores also in the major towns, however, currently their turnover in drug formulations in quite limited. Based on the figures of procurement by Ministry of Health during last 3 years, it is observed that setting up a formulation unit for the manufacture of tablets and capsules would be viable in Bhutan. The market is likely to further expand with the growth in demand from the government as well as private medical stores who are mostly selling branded drug formulation. As the Government of Bhutan would be the major buyer for the products of the unit, the project need to mainly focus on meeting the various parameters of government supplies viz packaging of tablets in bulk package to cut down the cost and be competitive with the existing sources of supply. The unit also needs to tap the open market through sales of formulation to medical stores. Presently there are no pharmaceutical units in Bhutan and government being the major buyer, there exist bright prospects for the unit to capture substantial market share in the supply of drug formulations.

4. Annual production capacity recommended	Pharmaceutical tablets – 1200 lacs Pharmaceutical capsules – 100 lacs		
5. Land and building requirement	Plot area 1000 sq. mts Built up area 800 sq mts		
6. Power requirement	72 KWH		
7. Main machinery	Mechanical sifter Powder and mass mixer Multi mill Granulator Double cone blender Tray drier with 48 trays Peristantic pumps Rotary tablet machine De dusting unit Coating machine with SS coating pan Strip packing machine		
8. Manpower requirement	Manager Manufacturing chemist Production supervisor Office staff & marketing executive Skilled workers Unskilled workers	– – – – – –	1 1 2 5 10 7
9. Total project cost	Rs. 126.03 lacs		
10. Project implementation period	14 months		
11. Means of finance	Debt - Rs. 88.22 lacs (70%) Equity - Rs. 37.81 lacs (30%)		

12. Break up of cost of project	Machinery	-	Rs. 45.40 lacs
	Construction cost	-	Rs. 48.00 lacs
	Misc. fixed assets	-	Rs. 2.00 lacs
	Pre-operative exp.	-	Rs. 3.00 lacs
	Training expenses	-	Rs. 0.45 lacs
	Interest	-	Rs. 11.86 lacs
	Working capital	-	Rs. 15.32 lacs
	Total	**-**	**Rs. 126.03 lacs**
13. Annual sales turnover	Rs. 186 lacs		
14. Financial analysis	IRR – 36% on equity		
	IRR – 23% on investment		
	NPV – Rs. 76.36 lacs (discount rate of 12%)		
	Pay back period – 3 years 6 months		
	Project break-even – 62%		

CHAPTER 2 – JUSTIFICATION OF THE PROJECT

2.1 Project Concept

The project is for carrying out the detailed feasibility analysis for setting up a drug formulation unit for the production of tablet, capsules and powders mainly to cater to the government demand of hospital supplies.

2.2 Project Justification

In Bhutan, over the last four decade the health care sector has undergone a radical change. Bhutan today has a well developed decentralized system of health care. The health care network of hospitals, Basic Health Units (BHUs) and Out Reach Clinics (ORCs) deliver free health care to over 90 per cent of nation's highly dispersed population. As off now, there are 29 hospitals, 176 Basic Health Units (BHUs) and over 514 Outreach Clinics (ORCs) spread over 201 gewogs providing primary health care services. A total of 2,749 health personnel of different categories serve in different hospitals. Besides, the allopathic system, there exists a well established network of indigenous medical facilities under the Institute of Traditional Medical Services that has basically three functions; medical services for outdoor patients; collection and manufacturing of indigenous medicines.

In view of the growth in the health care facilities network, increase in the demand for various medicines and non-medicine items, upcoming industrial development of Bhutan, it has been realized that some of the requirements for hospital supplies could be manufactured in the country. This approach would provide higher level of efficiency and sustainability to health care services sector as well as help in the industrial development of the country.

Based on the study of entire spectrum of hospital supplies viz. medicines and non-medicines items of supplies, their current level of demand, future demand projections, frequency of recurrence of the demand, major centres of requirement, present system of supplies, comparative advantages of factor inputs and markets, etc. It was found that there is enough justification for setting up a project for the manufacture of oral drug formulations in tablet and capsule form. The major formulations identified included paracetamol, anta-acid, iron-folic acid and vitamin B complex.

Drug can be administered through various modes and through various dosage forms viz. oral, parenteral and topical to produce localized system effect. Oral route of drug administration through use of 'oral solids' is the most widely used route of drug administration. The term oral solids refers to three major groups of dosage forms, the compressed tablet, molded tablets, hard shell capsule, and soft shell capsule, together with other less frequently used dosage forms such as the powder. When considered together, they are easily the most popular group of dosage forms. They account for in

excess of 70% of all dispensed National Health Service prescriptions dispensed in the United Kingdom, as well as a significant proportion of 'over-the-counter' sales. It is estimated that the pharmaceutical industry produces approximately 75% of its solid dosage form as compressed tables, 23% as hard gelatin capsules, and 2% of soft elastic capsules. A similar degree of usage is encountered world wide of the three dosage forms. The tablet is the most commonly used, followed by the hard shell capsule and then the soft. There are several reasons for the popularity of this group of dosage forms:

- They all employ the oral route of administration, which is generally the most acceptable route.
- They permit a high accuracy of dosage.
- The dose of the active drug is contained in a relatively small volume. Thus a concentrated dosage form is produced, leading to ease of packaging, transport, storage, and eventual administration.
- All three dosage form is essentially water free and hence loss of potency due to hydrolysis should be minimized. Packaging of the products into strip or blister packs should also enhance stability.

In case of Bhutan medical supplies also the oral solids especially tablets, capsules and powders constitute the major segment of medicine supplies. The important being paracetamol tablets, anta-acid tablets, iron folic acid tablets and ORS. Besides allopathic medicine a large number of traditional drugs formulation are used in Bhutan in the form of tablets. There are no indigenous facilities for the production of allopathic medicines including tablets, capsules or powders in Bhutan and the entire requirement is being sourced through imports from India and other countries. However, Institute of Traditional Medical Services (ITMS) has a pharmaceutical unit to produce traditional medicine in various dosage forms. The manufacturing facilities for traditional medicine formulation are being corporatarised and upgraded.

Keeping in view, the large demand of tablets, capsules and powder in Bhutan and there being no indigenous manufacturing facilities, the project has been drawn for the manufacture of these dosage forms based on imported bulk drugs. It is envisaged that the proposed production unit shall have the modern facilities for the production of various allopathic drugs in the form of tablets, capsules and powders. The bulk drugs and other ingredients are proposed to be imported. The production unit is designed to meet the domestic demand viz. Government Hospital supplies and open market sales through medical stores as well to export its produce to adjoining markets.

The detailed description of product, product range and technology used are given in subsequent chapters.

CHAPTER 3 – MARKET ANALYSIS

3.1 Demand and supply scenario

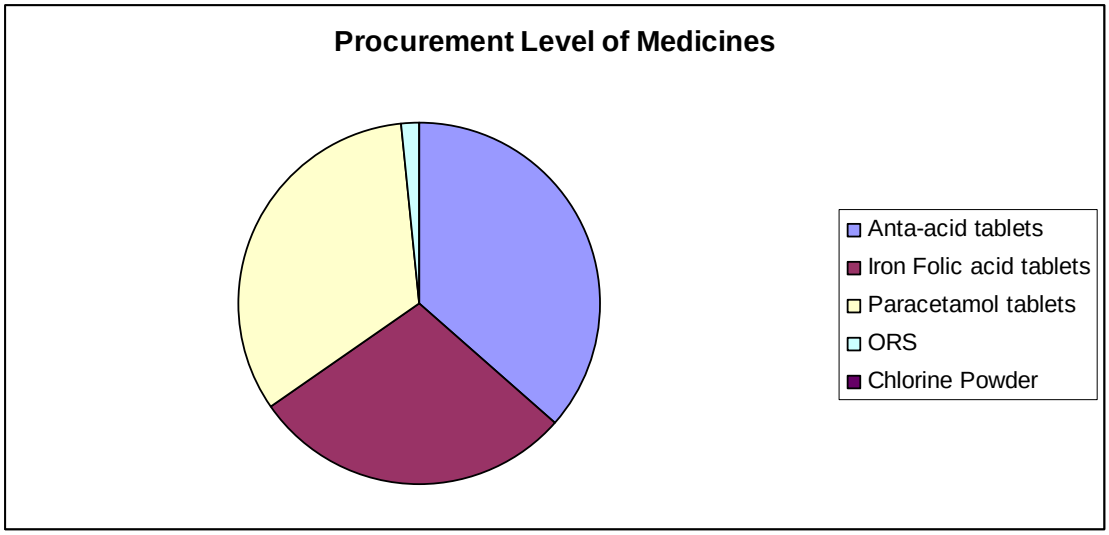
A wide range of products both medicines and non-drug items are required as consumables in hospitals and basic health units. Majority of these items are procured centrally by department of medical services and then supplied to hospitals while other items are procured directly by hospitals. The list of consumable items required by hospitals particularly medicines is quite exhaustive and the demand level keeps on changing depending on the requirements and health programmes conducted by the government. However, certain items are consistently required in large quantities and constitute major portion of hospitals supplies in terms of consumables. Some of these items being procured centrally include the following.

- Medicines mainly tablets
- Absorbent cotton, gauge & bandages
- Disposable syringes
- Glucose saline
- Surgical gloves

The data relating to the procurement of tablets mainly paracetamol tablets, anta-acid tablets and iron-folic tablets which constitute the major supplies as available from Drugs, Vaccine & Equipment Division, Department of Medical Health Services is given below:

Procurement Level of Medicines (Tablets & Powders):

	2005-06			2006-07			2007-08		
Item	Unit Rate	Quantity	Total Amount	Unit Rate	Quantity	Total Amount	Unit Rate	Quantity	Total Amount
Antacid	0.11	8824000	970640.00	0.13	12897000	1631470.50	0.13	15127000	1895413.10
Iron Folic Acid tab	0.10	7212000	696513.20	0.10	10000000	969600.00	0.09	12000000	1130112.00
Paracetamol 500mg tab	0.09	11107000	1028036.15	0.13	17273000	2323218.50	0.11	13821000	1513399.50
ORS	0.00	0	0.00	1.93	879700	1693422.50	2.30	664700	1528810.00
Chlorine powder	13.00	7223	93899.00	12.30	16995	209038.50	14.60	9565	139649.00
TOTAL			2789088.35			6826750			6207384



It would be observed that the annual requirement of above said 3 types of tablets is around 40 million numbers. Considering the requirement of other tablets by the government and the requirement of open market from medical stores, the current demand level of different types of tablets is estimated to be around 55-60 million tablets.

The demand estimates for pharmaceutical tablets and powders, as mentioned above, have been worked out based on the actual procurement figures as available from Ministry of Health. The installed capacity of the unit has been decided keeping in view the existing demand level, projected growth in the demand and the open market requirement being met through sales by medical stores. It has also been considered that the proposed unit could marketed some of its production mainly tablets in the adjoining markets through exports. Taking into consideration the current demand level, future growth in the demand and the possibilities of export to adjoining markets, the installed capacity of the unit for tablets has been kept at 120 million tablets per annum.

3.2 Competitive Advantages

Presently, the entire requirement of drug formulations is being imported mainly by the Ministry of Health as there is no indigenous production. Setting up of the unit for the production of pharmaceutical tablets and capsules would be beneficial both for the health care authorities as well as for the production unit. The competitive advantage factors of the indigenous production over the imported pharmaceuticals could be summarized as under: -

- Better inventory control management leading to lower cost of production, the production can be planned as per demand.
- The concerned agency / authority in the government could also minimize their inventory cost as the products could be procured at a short notice from the unit as per demand.

- Against the bulk order from the Ministry of Health, the possibilities of direct supplies of tablets and capsules by the unit to hospitals based on their demand could also be explored resulting in saving in the transport and the inventory and storage costs.
- The local production would also enable the medical stores to have better inventory control as they can procure the formulations as per their requirement.
- Quality control from raw materials to finished products and facility for strict compliance of the provisions of GMP.
- Direct purchase of raw materials viz basic drugs and diluents at most competitive rates leading to lower input cost.
- Lower cost inputs in terms of power, transport and labour.
- Value addition leading to saving of foreign exchange.

Keeping in view these competitive advantage factors, it is envisaged that the unit would be able to capture a substantial market both in government supplies as well as in the open market sales.

3.3 Marketing Strategy

As the Ministry of Health, Government of Bhutan would be the major buyer for the products of the unit, the project needs to mainly focus on meeting the various parameters of the government requirement vis packaging of tablets in bulk with a view to cut down the cost and be competitive with the existing sources of suppliers. The unit also needs to adhere to the guidelines of GMP and install the production facilities as per GMP requirement. As compared to the existing demand levels, a higher level of production has been envisaged primarily with a view to meet the requirement of future growth in demand and also to achieve the economics of production and be competitive with the existing channels of supply. It may however be pertinent to mention that the unit needs to plan and implement its activities in close cooperation with the concerned authorities in the government and strive at meeting their requirements of quality standards as a government would be the major customer for the produce of the unit. For supplies to the medical stores, the unit needs to install strip packaging and blister packaging machine for tablets and capsules. The unit needs to take up a market development program for marketing tablets and capsules to medical stores through medical representatives as per normal practice adopted by the drug formulation companies. In the existing scenario of drug formulation market, the following marketing strategies need to be adopted by the unit: -

- Marketing of drug formulations to concerned department in Ministry of Health for onward distribution to hospitals specially in bulk packs.
- The unit needs to get its products approved as per relevant standard and specifications of the Ministry of Heath, Government of Bhutan.
- Sales to medical stores in strip packaging through medical representatives.
- Export to adjoining markets in India and other countries.

3.4 Product range and target markets

The project has been drawn to set up a pharmaceutical unit for the manufacture of oral solids mainly tablets, capsules and powders. The manufacture of all these dosage form requires the use of specialized machines which have been detailed in subsequent chapters. These dosage forms have been selected because of relatively simple manufacturing operations involved and possibilities of production of large quantities over a short period. For example, it is possible to manufacture tablets ranging from few thousand per hour to one million for hour by using different machines. Similarly, it is possible to fill hard gelatin capsule up to 150,000 per hour. This chapter describes the type and characteristics of tablets and capsules.

3.4.1 Tablets

Tablets may be defined as solid pharmaceutical dosage forms containing drug substances with or without suitable diluents and prepared either by compression or molding methods. The British Pharmacopoeia States that tablet are solid preparation each containing a single dose of one or more active ingredients are obtained by compressing uniform volume of particles. They have been in widespread use since the latter part of the 19th century and their popularity continues. In the modern days also the tablet are undoubtedly the most popular mode of presentation of solid dosages form intended for oral administration.

Tablets remain popular as a dosage form because of the advantages afforded both to the manufacturer viz simplicity and economy of preparation, stability, and convenience in packaging, shipping, and dispensing and the patient viz. accuracy of dosage, compactness, portability, blandness of taste, and ease of administration. Their popularity is increasing due to the following advantages:

- Tablets are easy to carry
- Tablets are easy to swallow
- Tablets are attractive in appearance
- Unpleasant taste can be masked by sugar coating
- Tablets do no require any measurement of dose. The strip or blister packing has further facilitated the process of taking the dose by the patient. Moreover, it provides a sealed covering which protects the tablets from atmospheric conditions like air, moisture and light etc.
- Some of the tablets are divided into halves and quarters by drawing lines during manufacturing to facilitate breakage whenever a fractional dose is required.
- An accurate amount of medicament even if very small can be incorporated.
- Tablets provide prolonged stability to medicament.
- The incompatibilities of medicaments and their deterioration due to environmental factors are less in tablet forms.
- Since they are generally produced on a large scale therefore their cost of production is relatively low, hence economical.

The tablets vary greatly is shape, size and weight which depends upon the amount of medicaments and the mode of administration. Most commonly, the tablets are disk shaped with convex surface. Although tablets are more frequently discoid in shape, they also may be round, oval, oblong, cylindrical, or triangular. They may differ greatly in size and weight depending on the amount of drug substance present and the intended method of administration. Tablets are divided into two general classes, whether they are made by compression – compressed tablets or molding- molded tablets or tablet triturates (TT). Compressed tablets are usually prepared by large-scale production methods while molded tablets generally involve small-scale operation.

These two types of tablets are further sub-classified as under:

3.4.1.1 Compression Molded Tablets

These tablets are manufactured by using compression technique and mainly comprises of the following types:-

Compressed Tablets: These tablets are formed by compression and contain no special coating. They are made from powdered, crystalline, or granular materials, alone or in combination with binders, disintegrants, lubricants, diluents, and in many cases, colorants.

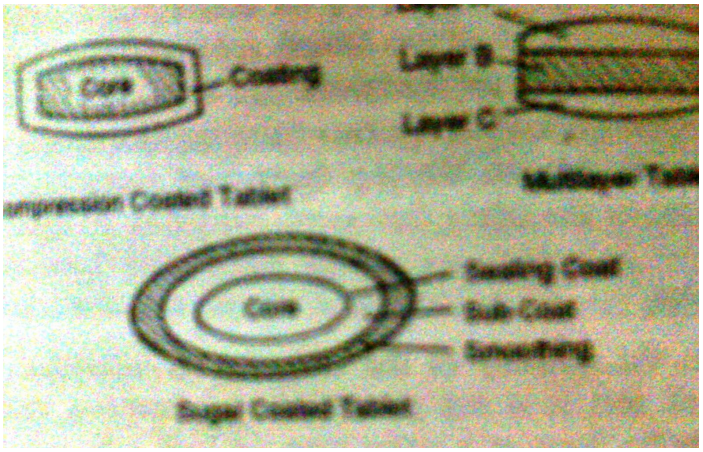
Sugar-Coated Tablets: These are compressed tablets containing a sugar coating. Such coatings may be colored and are beneficial in covering up drug substances possessing objectionable taste or odors and in protecting materials sensitive to oxidation.

Film-Coated Tablets: These are compressed tablets which are covered with a thin layer or film of a water soluble material. A number of polymeric substances with film-forming properties may be used. Film coating imparts the same general characteristics as sugar coating with the added advantage of a greatly reduced time period required for the coating operation.

Enteric-Coated Tables: These are compressed tablets coated with substances that resist solution in gastric fluid but disintegrate in the intestine. Enteric coatings can be used for tablets containing drug substances which are inactivated or destroyed in the stomach, or those which irritate the mucosa, or as a means of delayed release of the medication.

Multiple Compressed Tablets: These compressed tablets are made by more than one compression cycle.

Layered Tablets: Such tablets are prepared by compressing additional tablet granulation on a previously compressed granulation. The operation may be repeated to produce multilayered tablets of two or three layers. Special tablet presses are required to make layered tablets.



Press-Coated Tablets: Such tablet, also referred to as dry coated, are prepared by feeding previously compressed tablets into a special tableting machine and compressing another granulation layer around the preformed tablets. They have all the advantages of compressed tablets, viz. slotting, monogramming, speed of disintegration, etc. while retaining he attributes of sugar-coated tablets in masking the taste of the drug substance in the core tablets.

Controlled –Release Tablets: Compressed tablets can be formulated to release the drug substance in a manner to provide medication over a period of time. There are a number of types which include delayed action tablets in which the release of the drug substance is prevented for an interval of time after administration or until certain physiological conditions exist; repeat action tablets which periodically release a complete dose of the drug substance to the gastrointestinal fluids; and the extended release or sustained release tablets which continuously release increments of the contained drug substance to the gastrointestinal fluids.

Tablets for Solution: These are compressed tablets to be used for preparing solutions or imparting given characteristics to solutions. These tablets should be labeled to

indicate that they are not to be swallowed. Examples of these tablets are Halazone tablets for solution and Potassium Permanganate Tablets for solution.

Effervescent Tablets: In addition to the drug substance, these contain Sodium Bicarbonate and an organic acid such as Tartaric or Citric. In the presence of water, these additives react, liberating carbon dioxide which acts as a disintegrator and produces effervescence. Except for small quantities of lubricants present, effervescent tablets are soluble.

Compressed Suppositories or Inserts: Vaginal suppositories, such as Metronidazole Tablets, are prepared by compression. Tablets for this use usually contain lactose as the diluents.

Buccal and Sublingual Tablets: These are small, flat, oval tablets. Tablets intended for buccal administration by inserting into the buccal pouch dissolve or erode slowly; therefore they are formulated and compressed with sufficient pressure to give a hard tablet. Progesterone Tablets may be administered in this way. Sublingual tablets such as those containing nitroglycerin, isoproterenol hydrochloride, or erythrityl tetranitrate are placed under the tongue. Sublingual tablets dissolve rapidly and the drug substances are readily absorbed by this form of administration.

Chewable Tablets: These are the tablets which are required to be broken and chewed in between the teeth before ingestion. These tablets are given to the children who have difficulty in swallowing and to the adults who dislike swallowing. A number of antacid tablets and multivitamin tablets are prepared as chewable tablets.

For the preparation of chewable tablets mannitol is used as a base. It is a white crystalline, chemically inert, nonhygroscopic, thermostable powder and is as sweet as that of glucose. It does not have any objectionable effects but since it is expensive so ti cannot be used in tablets of low cost, therefore other substances like sorbitol lactose, chocolate powder, dextrose and glycine can be substituted in place of mannitol.

Lozenge Tablets: These tablets should not disintegrate in the oral cavity but should dissolve slowly in the mouth to produce continuous effect on the mucous membrane of the throat. They can be prepared by molding as well as by compression method. The lozenges prepared by compression are known as lozenge tablets.

3.4.1.2 Molded Tablets or Tablet Triturates

Tablet triturates are usually made from moist material using a triturate mold which gives them the shape of cut sections of a cylinder. Molded tablets are small disk shape tablets which are produced by forcing the soft mass in to the cavities of the mold. Generally potent medicaments and highly toxic drugs in small doses are used for producing molded tablets. These comprises of the following types;

Dispensing Tablets: These tablets are prepared for providing an accurate and convenient quantity of a drug that can be incorporated readily in compounding other dosage forms e.g. liquids, powders, or capsules thus eliminating the necessity of

weighing small quantities of potent substances. These tablets are solely designed to provide a convenient quantity for administration as a dosage form because sometimes they contain very potent drugs which may prove fatal.

Hypodermic Tablets: Hypodermic tablets are soft readily soluble tablets which are made in a tablet triturate mould. They are used for preparing solutions to be injected, therefore in selecting the materials used for preparing the hypodermic tablets care must be taken that they should be completely and readily soluble and no insoluble particle should be present. They should be free from bacterial contamination and proper precautions should be taken during molding regarding contamination and cleanliness.

Since the solutions prepared from hypodermic tablets are rarely sterile and a number of sterile parenteral solutions are now available therefore the use of hypodermic tablets for preparing solution for injections is being discouraged.

3.4.2 Capsules

Capsules are solid dosage forms in which the drug substance is enclosed in either a hard or soft, soluble container or shell of a suitable form of gelatin. According to *British Pharmacopoeia,* the capsules are defined as solid preparation with hard soft shells, of various size, shapes and capacities, containing a single dosage of active ingredient. The capsules are intended for oral administration. The encapsulation of medicinal agents remains a popular method for administering drugs. In prescription practices the use of hard gelatin capsules permits a choice in prescribing a single drug or combination of a drug at the exact dosage level considered best for the individual's patients. This flexibility is an advantage over tablets. Some patient finds it easier to swallow capsules than tablets and prefer this form of dosages. The preference of promoted pharmaceutical companies to market the product in capsules form even though the product has already been produced in tablets forms.

The capsules form of dosage offers the following advantages:-

- Capsules are tasteless, odorless and can be easily administered.
- They are elegant and attractive in appearance.
- The drugs having unpleasant order and taste are enclosed in tasteless shell.
- Can be filled quickly and congenitally, physician can the dosage and combination suiting to individuals patient.
- Capsules are to easy handled and carry.
- The capsules forms are dosage is readability economically.

However they are certain disadvantage associated with this form of dosages these include the following:

- The drugs which are hygroscopic are not suitable for filling into capsules. They will absorb the water present in the shell rendering it brittle.
- The concentrated salutations which require prior devaluation are unsuitable for capsules.

- Based on the type of gelatin shell and the physical form of medicine filled in the shell, the capsules are classified in two categories vis hard gelatin capsules and soft capsules.

3.4.2.1 Hard Shell Capsule:

The hard shell capsules are also referred to as dry-filled capsule (DFC). The hard capsules as a dosage form consist for two distinct parts, the shell and the contents. The shell is almost invariably composed of gelatin and comprises of two sections, the body and the cap. Both are cylindrical, sealed at one end. The Body is filled with particulate solid and the cap capsules than is closed by bringing cap and body together.

3.4.2.3 Soft Shell Capsules:

These capsules are soft and elastic in nature which are prepared from gelatin and water to which glycerin, sorbitol or propylene glycol has been added as a plasticizer which make the capsules flexible. They usually contain a preservative to prevent the growth of bacteria and fungi. These capsules are available in the number of shapes and sizes e.g. spherical, ovoid, cylindrical and tubes. The spherical capsules are also known as “pearls”. The contents of the soft capsules may very from 0.1 ml to 30 ml.

The soft gelatin capsules differ from hard capsules that the latter are manufactured in two steps where the shells are made on one type of machine and filling is done one another machine. Whereas soft capsules are formed and filled in one

continuous operation on semi-automatic and automatic machines. They are hermetically sealed.

The capsules are used for filling liquids and semi-solids. Vitamin preparations such as halibut liver oil, vitamin A and d and multivitamins are conveniently dispensed in soft capsules. They are also used for containing eye, ear, nose and throat preparations. Ophthalmic ointments are frequently packed in unit dose capsules.

3.4.3 Powder and Granules

Powders are mixture of finely divided solids intended for oral administration, and comprise the active ingredients plus exvipients (such as diluents, sweeteners, and dispensing agents) where necessary. They are usually mixed with water or other suitable liquid before administration.

Powders containing non-potent materials are often supplied in bulk, with directions to administer a specific volume as a dose. An alternative use for bulk powder is as the basis for the preparation of liquid mixtures, the solid ingredients in the powder being in the same proportions as they occur in the liquid preparation. Thus the packaging and transport costs of the liquid ingredients are avoided. Powder for mixtures may be presented in bulk, from which the appropriate quantity of powder is weighed, or in packs, each containing sufficient powder to prepare a given volume of mixture.

Because of the possibility of segregation occurring within bulk powders during storage or when subjected to vibration, care must be taken to ensure homogeneity before use. Examples include powders for Kaolin mixture BP and Magnesium Trisilicate mixture BP. For more potent drugs, or where accuracy of dosage is more important, individually packaged powders (either in sheets of paper or in sachets) are used. The minimum weight of such powders is 120 mg, and so dilution of the drug, usually with lactose is often necessary. Though not a frequently encountered dosage form, the individually wrapped powder offers the opportunity for administration of potent drugs in doses that are not commercially available in tablet or capsule.

By choosing appropriate ingredients, powders may be soluble, dispersible, or effervescent. Granular materials may also be used as dosage forms for oral administration, being either swallowed as such, chewed, or dispersed in water or a suitable liquid before consumption. They too can be presented as bulk packs or as individually packaged doses.

3.5 Quality Control & Standardization

A). Tablets: The following standards or quality control tests are carried out on compressed tablets: -

- Diameter size and shape
- Uniformity of weight
- Thickness
- Hardness
- Friability
- Percentage of medicament
- Rate of disintegration

11.1.1. Diameter size and shape: The diameter size and shape of tablets depends on the die and punches selected for making the tablets. The tablets of various sizes and shapes are prepared but generally they are circular with either flat or biconvex faces.

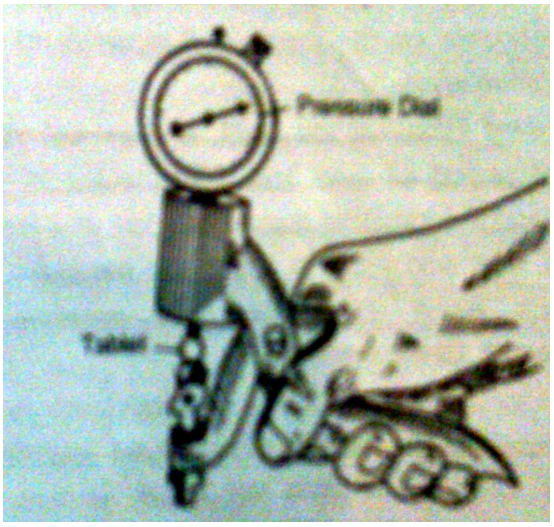
11.1.2. Uniformity of weight: It is desirable that all the tablets of a particular batch should be uniform in weight. If any weight variation is there, that should fall within the prescribed limits (generally ± 10% for tablets weighing 120 mg. or less, ± 7.5% for tablets weighing 120 mg to 300 mg and ± 5% for tablets weighing more than 300 mg). The test is considered correct if not more than two tablets fall outside this range if 20 tablets are taken for the test and not more than one tablet falls outside this range if only ten tablets are taken for the test. The difference of weight in tablets can lead to variation in doses. Therefore all the tablets of a batch must conform to this test.

For carrying out this test generally 20 tablets at random are taken and weighed. The average weight is calculated, than each tablet is weighed individually and weight

noted. The weights of individual tablets are then compared with the average weight already calculated and see that not more than two tablets fall outside the range.

Thickness: The thickness of a tablet can vary without any change in its weight. This is generally due to the difference of density of granules, pressure applied for compression and the speed of compression. The thickness of a tablet can be determined with the help of micrometer calipers. The thickness variation limits allowed are + 5% of the size of the tablet. The variation in thickness leads to counting and packing problems.

Hardness of tablet: The hardness of tablet depends on the weight of the material used, space between the upper and lower punches at the time of compression and pressure applied during compression. The hardness also depends on the nature quantity of exvipients used during formulation. Tablet hardness can roughly be determined by holding the tablet in between the figures of the hand and throwing it lightly on the floor, if it does not break it indicates that proper hardness has been obtained. A number of harness testers are used for determining the tablet hardness but Monsanto hardness testers and Pfizer hardness testers are commonly used.



Friability: Friability test is performed to evaluate the ability of the tablets to withstand abrasion in packing, handling and transporting. The instrument used for this test is known as Friability Test Apparatus or Friabilitor. It consists of a plastic chamber which is divided into two parts and revolves at a speed of 25 rpm. A number of tablets are weighed and placed in the tumbling chamber, which is rotated for four minutes or for 100 revolutions. During each revolution the tablets fall from a distance of six inches to undergo shock. After 100 revolutions the tablets are again weighed and the loss in weight indicates the friability. The acceptable limits of weight loss would not be more than 0.8 per cent.

Percentage of medicament: This test is performed to ensure that every tablet, coated or uncoated must contain the stated amount of medicaments within the prescribed limits. A number of tablets from a batch are selected at random and assay procedures are carried out according to the monographs given in the official books. The results obtained must be within the prescribed percentage limits.

Rate of disintegration: The disintegration test is performed to find out that within how much time the tablet disintegrates. This test is very important and necessary for al the tablets, coated or uncoated to be swallowed because the dissolution rate depends upon the time of disintegration which ultimately affects the rate of absorption of drugs. The apparatus used for this test is known as disintegration test apparatus. This apparatus consists of a glass or plastic tube which is open at one end and the other end is fitted with a rust proof No. 10 mesh sieve.

Dissolution test: The rate of dissolution of a solid drug plays an important role in the absorption and physiological availability of the drug in the blood stream. Therefore determination of dissolution rate of any solid drug is very necessary. For this purpose there are a number of tests available in the literature but none is official. This test is performed for tablets and capsules when stated in the individual drug monographs. The apparatus for dissolution test consists of (i) a cylindrical stainless steel basket which is attached to the end of the stirrer shaft (ii) a 1000 ml vessel made of glass or other inert, transparent material fitted with a cover having four holes, one for the shaft of the stirrer second for placing the thermometer and remaining two for removing the samples (iii) a variable speed motor driven stirrer which can rotate at a speed of 25-150 revolutions per minute (iv) a suitable thermostatically controlled water bath to maintain the temperature of the dissolution medium at a temperature of 37^0 C + 0.5 ^{0}C.

The empty capsules are filled into the loading trays, which is then placed over the bed. By operating the handle, the bodies of the capsules are locked and caps separated in the loading trays itself, which is then removed by operating the lever. The weighed

amount of the drug to be filled in the capsules is placed in powder tray already dept in position over the bed. Spread the powder with the help of a powder spreader so as to fill the bodies of the capsules uniformly. Collect excess of the powder on the platform of the powder tray. Lower the pin plate and over it downward so as to press the powder in the bodies. Remove the powder tray and place the caps holding tray in position. Press the caps with the help of plate with rubber top and operate the lever to unlock the cap and body of the capsules. Remove the loading tray and collect the filled capsules in a tray. With 200 hole machine about 5000 capsules can be filled per hour and with 300 hole machine 7500 capsules can be filled per hour.

B). Capsules

Whether capsules are produced on a small or large scale all of them are required to pass not only the disintegration test, weight variation test and percentage of medicament test but a visual inspection must be made as they roll off the capsule machine onto a conveyor belt regarding uniformity in shape, size, color and filling. As the capsules move in front of the inspectors the visibly defective or suspected of being less than perfect are picked out. If the number of defective capsules is large it may be due to some fault in the capsule-filling machine, which must be corrected.

The hard and soft gelatin capsules should be subjected to following test for their standardization.

- Shape and size.
- Colour
- Thickness of capsules shell
- Leaking test for semi solid and liquid ingredients from soft capsules.
- Disintegration test.
- Weight variation test
- Percentage of medicament test

In official books the following quality control test are recommended for capsules:

Disintegration test: For performing disintegration test on capsules, the tablet disintegration test apparatus is used but the guiding disc may not be used expect that the capsules float on top of the water. One capsule is placed in each tube, which are then suspended in the beakers to move up and down for 30 minutes, unless otherwise stated in the monograph. The capsules pass the test if no residue of drug or other than fragments of shell remains on No. 10 mesh screen of the tubes.

Weight variation test: 20 capsules re taken at random and weighed. Their average weight is calculated. Then each capsule is weighed individually and their weight noted. The capsules pass the test if the weight of individual capsule falls within 90 –110% of the average weight. If this requirement is not met, then the weight of the contents for each individual capsule is determined and compared with the average weight of contents. The contents from the shells can be removed just by emptying or with the help of small

brush. From soft gelatin capsules the contents are removed by squeezing the shells which has been carefully cut. The remainder contents are removed by washing with a suitable solvent. After drying the shells, they are weighed and the content weights of the individual capsules are calculated. The requirements are met if (a) not more than 2 of the differences are greater than 10% of the average net content and (b) in no case the difference is greater than 25%.

Contents uniformity test

This test is applicable to all capsules, which are meant for oral administration. For this test, a sample of the contents is assayed as described in individual monographs and the values calculated which must comply with the prescribed standards.

CHAPTER 4 - RESOURCES

4.1 Main Resources

The main resources for the production of tablets, capsules and powder include the following:

- Land and building
- Plant and machinery
- Basic drugs commonly known as therapeutic ingredient
- Formulation additives viz diluents, binders, granulating agents, lubricants, etc.
- Power
- Skilled and non-skilled workers

It has been envisaged in the project the land for the project would be available on lease basis from Government of Bhutan and the building as per standard requirements has to be constructed for the formulation unit. The parameter of GMP has to be kept in view while finalizing the building plans. There is a requirement of manufacturing chemist and a person with sufficient experience in the manufacture of drug formulation need to be employed. The plant and machinery has to be imported as per details given in the project. In the initial phase, some experts viz manufacturing chemist and production supervisor has to be brought from India who in turn would be able to train the local staff over a period of time. The production supervisors also initially have to be employed from outside so as to maintain the quality standard of the product. The experts from the machine suppliers could also help in training the local staff on operations of machines. The drug formulations are required to be manufactured as per IP, BP & USP standards and in compliance to the standards to the Ministry of Health, Government of Bhutan.

4.2 Details of raw materials and consumables

In addition to basic drug or a combination of drugs commonly known as therapeutic ingredient or active ingredient, the tablet consists of a number of inert ingredients which are called excipients or additives. These additives are added to give the qualities of a good tablet. These additives are formulated in the form of powder or granules before they are made in tablet form. In case of capsules also the active ingredient are invariably formulated with the addition of excipients or additives. However, their use is move predominant in the production of tablets. These additives are classified in accordance with the function they play in the preparation of tablets or in imparting certain characterizes of the tablets. These included the following.

4.2.1 Diluents

When the quality of the drug for an individual dose is very small and it is not practicable to compress such small amount in the form of a tablet then the inert substances which are added to increase the bulk of powders to be easily compressed

are known as diluents. Various diluents used are: lactose, sodium chloride, starch, powdered sucrose, mannitol, calcium carbonate, calcium sulphate, calcium phosphate etc.

4.2.2 Binders

Some substances which are available in the crystalline form can be compressed directly but majority of the drugs will have to be converted to granules before compression. The agents used during granulation to impart cohesiveness to the powdered substances are known as binders. They keep the tablet intact after compression. Various commonly used binders are: starch, acacia, tragacanth, gelatin, glucose, lactose, sucrose, methyl cellulose etc.

4.2.3 Granulating agents

Granulating agents are the substances which are added to powders during granulating process to convert fine powders into granules. The quantity of proper granulating agent to be incorporated is very critical. Insufficient quantity of granulating agent may lead to poor adhesion, soft tablets and 'capping', whereas excessive quantity may lead to hard tablets with greater disintegration time. In addition the wet screening may be more difficult if excessive granulating agent is present. The commonly used granulating agents are: water, mucilages of acacia, tragacanth and starch; liquid glucose, syrup and alcohol in various dilutions.

4.2.4 Disintegrating agents

Disintegrating agents or disintegrators are the substances or a mixture of substances which are added to tablets to facilitate their disintegration or breaking apart into small particles in G.I.T. after administration, thus facilitating dissolution. Generally two types of disintegrating agents are used (i) substances which swell up when they come in contact with moisture (ii) substances which react with effervescence when they come in contact with moisture.

The most popular and commonly used disintegrating agents of first type are maze starch and potato starch. These starches have great affinity for water and swell up when they come in contact with water thus breaking the tablet apart. The other disintegrating agents include veegum, methyl cellulose, agar, bentonite, carboxy methyl cellulose and citrus pulp. Some manufacturers use sodium lauryl sulphate alongwith starch as disintegrating agent. This produces better wetting of the granules resulting in faster dissolution rate of drugs.

The second type of disintegrating agents include a combination of sodium bicarbonate, citric acid and tartaric acid. When this combination comes in contact with moisture present in the stomach produces effervescence thus disintegration the tablet.

4.2.5 Lubricants

Lubricants are the substances which are added to granules before compression to improve the flow of granules from the hopper to the die cavity by reducing interparticle friction, to prevent adhesion of the powders to the surface of dies and punches thus reducing wear and tear of dies and punches and to facilitate the ejection of the tablet from the die cavity after compression. Commonly used lubricants are; magnesium stearate, calcium stearate, stearic acid and talc. Other materials such as cocoa butter, hydrogenated vegetables oils, liquid paraffin, hard paraffin, waxes and wax like materials may also be used as lubricants to prevent adhesiveness to the surface of dies and punches.

4.2.6 Colouring agents

Coloring agents are used to impart elegance to the tablets. Sometimes they are also used to identify the different types of tablets. Only the approved colours are used. These colours may be added either in the mixed powders before granulation or they may be dissolved in the vehicles used for making the granules. The latter procedure gives more uniform colour.

4.2.7 Flavouring agents

Generally flavours are added to all lozenges, chewable tablets and effervescence tablets. Volatile oils, volatile substances and fruit flavours are used for this purpose. The volatile substances are dissolved in a suitable organic solvent and sprayed over the granules before compression. Fruit flavours and spray dried beadlets are incorporated to the mixed powders before granulation.

4.2.8 Sweetening agents

Sweetening agents are added to the tablets which are required to be dissolved in the buccal cavity. The bases for their formulation are already sweet e.g. mannitol, lactose and sucrose. They impart sweetness of varying degree. The additional sweetness may be imparted by including additional quantity of sucrose and artificial sweetening agents like cyclamates and saccharin. But the use of cyclamates and saccharin have already been banned therefore sugar can be included to impart an acceptable taste.

Compared with tablets, powders for filling into hard gelatin capsules require the minimum of formulation efforts. The powder usually contains diluents such as lactose, mannitol, calcium carbonate, or magnesium carbonate. Since the flow of material is of great importance in the rapid and accurate filling of the capsule bodies, lubricants such as the stearate are also frequently used.

4.3 Quality Standards of raw materials

Almost entire range of raw materials is required to be imported including basic drugs and packaging materials. All raw materials are required to meet IP, BP and USP standards.

4.4 Comparative analysis of sources and prices of critical inputs & consumables

As mentioned earlier, various raw materials required for manufacture of pharmaceutical tablets, capsules and powders include the following: -

- Basic drugs / therapeutic agent / active ingredient
- Additives / excipients
- Packing materials viz bottles, strips and foils.

The main raw material for these products is basic drug which can be either imported directly from basic drugs manufacturing units in India on most competitive prices or through trade channels. The additives / excipients and packaging material could be sourced from wholesale dealers supplying these raw materials.

4.5 Recommended sources

A list of raw material supplier has been given in the Annexure II.

4.6 Annual requirement of raw materials

The annual requirement of various raw materials along with their prices has been given in the chapter 9 relating to cost presentation.

CHAPTER 5 – THE PLANT

5.1 Selection of technology

Different technologies and processes are used at various stages for the manufacture of tablets and capsules depending on the type of drug formulation. Similarly, different types of packaging techniques are employed keeping in view the type of drug formulation and target market. The details of manufacturing and packaging technologies for tablets and capsules are given below:

5.2 Technology for tablets

Compression molding is the most widely used technology for the manufacture of tablets. The project also envisages the use of compression molding technique. The manufacture of compressed tablets involves the following four process operations.

- Formulation & Granulation
- Compression
- Coating
- Packaging

5.2.1 Formulation & Granulation

In the manufacture of tablets, the particulate matter is invariably converted in the form of granules before its compression in to tablets. The granule offers the following advantages:

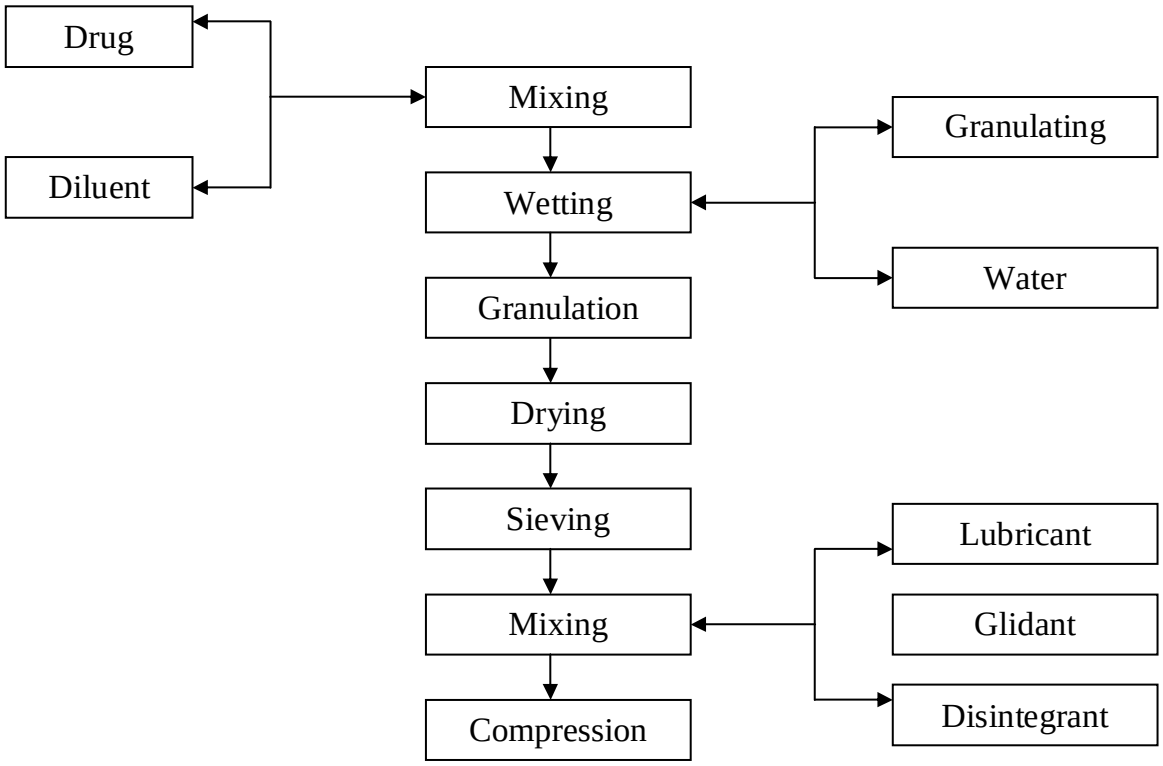
- Flow uniformly and quickly into the die of the tablet press.
- Cohere when subjected to a compressing force.
- Ensure that the finished tablet will be ejected from the die of the press quickly and easily.

The granulation is done by using either of the following two processes.

Wet Granulation: This is the most widely used method in the production of tablets. The steps involved are weighing, mixing, granulation, sieving the wet mass, drying, sieving the dried mass, lubrication and compression.

In this method, the crystalline substances are reduced to fine powder, they are mixed with other ingredients major portion of the disintegrating agent is incorporated and mixed uniformly. The mixed powder thus obtained are passed through a sieve. Dry binding agent if any added followed by the careful addition of granulating agent or binding solution. The addition of proper quantity of granulating agent is very important because if the quantity is less this will lead to poor adhesion, soft tablets and capping whereas the excessive quantity of binding agent will lead to the formation of a very hard

tablet which will take a longer disintegrating time. It may also be more difficult to pass the excessive wet mass through the sieves to get proper granules. After adding the proper quantity of the granulating agent to the powders they are mixed continuously until uniform mass is obtained. The wet mass so obtained is then passed through sieve. On large scale manufacturing various types of granulating machines can be used. The wet granules obtained after passing through the various sieves are spread in thin layers in trays and dried in an oven at a temperature not exceeding 60^0C. the dried granules are broken up and passed through a proper screen to obtain the granules of proper size. The granules are then mixed the other additives like the second portion of disintegrants, lubricants and flavoring agents etc. The blended granules are thus ready for compression. The process flow chart of wet granulation is given below:



Dry Granulation:

This method is also known as slugging, pre-compression or double compression method. In this method the blend of powder are compressed into slugs on specially designed tablet machines. These slugs are then broken to suitable size granules by passing through an oscillating granulator or other suitable device fitted with sieve. The resultant granules are mixed with lubricants and other necessary additives, and then they are compressed into finished tablets in the usual way.

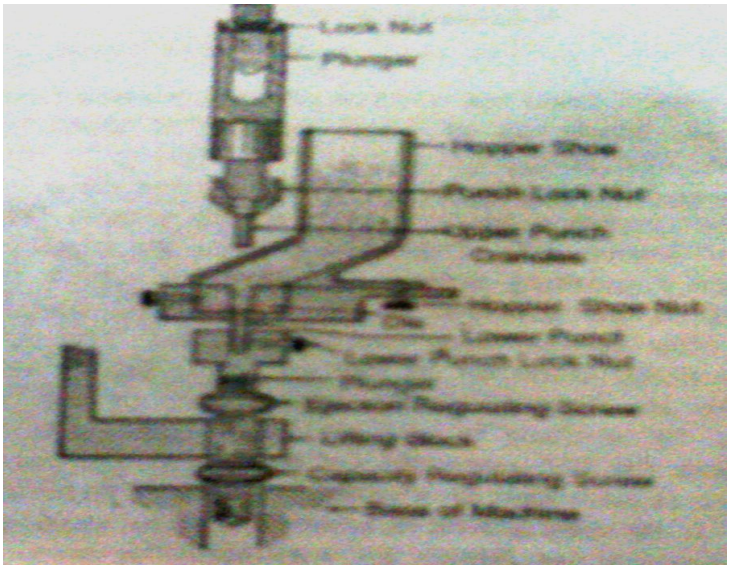
5.2.2 Tablet Compression

For the compression of granules in the form of tablets, various types of machines are used which are known as tablet making machines or tablet presses. Various types of machines so used are as follows:

- Single punch machines.
- Multi punch machines.
- Rotary tablet machines.
- High-speed rotary tablet machines.
- Multilayer rotary tablet machines.

Single Punch machines: In these types of machines one set of die and punch is fitted and only one tablet can be compressed at one time. They are used when small quantity of tablets are to be prepared. They may be hand operated or powder operated and with these machines 60 to 90 tablets per minute can be prepared.

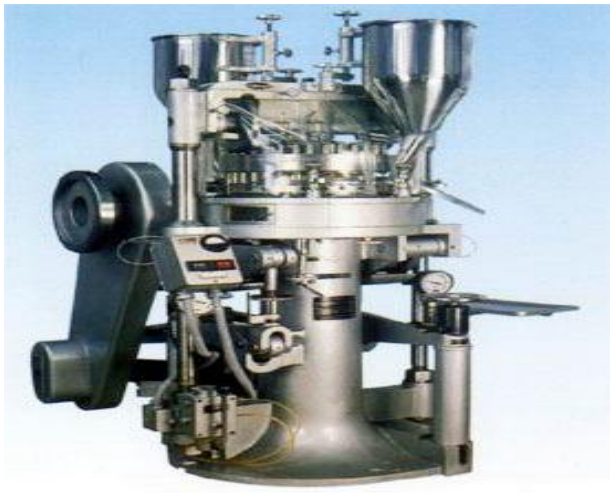
The granulated material ready for compression is placed in the hopper of the machine from where it feeds into the die, where it is compressed in between two punches, the upper punch and the lower punch. The lower punch is adjusted in such a way that it makes sufficient space in the die cavity to hold weight amount of the material so as to make the tablet of required weight and at the same time the top of the lower punch should be in level with the upper surface of the die for easy ejection of the compressed tablet from the die. The pressure required for compression adjusted from the upper punch. A number of train tablets are prepared and when the machine is adjusted correctly, it is locked in position and required numbers of tablets are prepared. When a large number of tablets are to be prepared, the materials can be put into the large feeding cup attached to the hopper. This avoids the frequent refilling of the hopper.



Multi Punch Machine: The construction and working of multi punch machines is exactly similar as that of hand operated single punch machines with the difference that a number of dies varying from 2-12 are fitted in the steel frame having exactly the same number of upper and lower punches. With multi punch machines, during one cycle instead of one tablet as many tablets are prepared as that of number of dies.

Rotary Tablet Machines: for large scale production, rotary tablet machines are used. The high speed rotary tablet machines are fitted with as many as 70 sets of dies and punches and can produce upto 10000 tablets per minute. The underlying principle of rotary tablet machine is that the dies and punches are mounted in a rotating holder (turret) which passes them in sequence through the filling, compression and ejection stages at a much faster speed whereby the output is increased to a great extent.

Multilayer Rotary Tablet Machines: with multilayer rotary tablet machines, tablets having one, two or three layers can be produced. They have the advantage that incompatible drugs can be compressed in different layers and separating these layers with an inert material. Sustained action preparations can also be prepared by this method.



5.2.3 Tablet Coating:

Tablets were originally coated for the sake of pharmaceutical elegance by improving their appearance, taste and stability. More recently coating has been used to control the site of drug release (enteric coating) and delay or prolong the release of drug from the dosage from (sustained action) and hence the absorption of drug or drugs present. The following types of tablets coating techniques are used:

Sugar coating: the most important is sugar coating of tablets. It is one of the oldest and most commonly used methods of coating the tablets on a commercial scale. It is used to mask the unpleasant taste and odour, to improve the appearance and to protect the ingredients from decompensation on exposure to air and moisture. The various stages involved in sugar coating are;

- Water proofing
- Subcoating
- Smoothing
- Colouring and finishing
- Polishing

Film coating:

A more recent method of coating the tablets is film coating. Although the film coated tablets are possible less elegant in appearance but they are considered more satisfactory than sugar coated tablets because in film coating various steps like water proofing, subcoating and smoothing are unnecessary thereby the coating time is reduced to a great extent, ultimately the cost of production is decreased and tablets of better strength are produced.

Compression coating:

This method is also known as press coating or dry coating as no water or any solvent is used in the coating. Only the dried granules are compressed around the pre-compressed tablets. This method is applicable to those drugs which are decomposed in the presence of moisture. Incompatible materials can be incorporated by pressing them in different coatings. One material can be compressed on the core and still another can be compressed on the core and the first coating. Similarly repeat action tablets can be prepared by coating the tablets with an appropriate material.

Enteric coating: Enteric coating is applied to the tablets which are required to pass the stomach as such but readily disintegrate in the intestines. The substances which are generally given enteric coating are those: (a) which are decomposed in the acidic medium of the stomach (b) which produce irritation in the stomach (c) the action of which is required only in the intestines (d) absorption of which takes place from the intestines (e) delayed action of which is required.

5.3 Technology for Capsules

The most commonly used dosages in capsules form hard gelatin capsules. In the manufacturer of hard gelatin capsules following process operations are used:

- Mixing / blending and granulation
- Capsules filling
- Capsules packing

The mixing / blending and granulation technologies and equipment are almost the same as employed in the production of tablets. The formulated drug composition is then filled in the hard gelatin capsules either by hand operator machine or semi automatic / automatic machines.

Hand operated capsules filling machines: Hand operating and electrically operating machines are used for filling the capsules mainly demand levels are small. In this process the empty capsules are filled into the loading tray which is then placed over the bed. By operating the handle, the bodies of the capsules are locked and caps separated in the loading tray itself which is then removed by operating the lever. The weighed amount of the drug to be filled in the capsules is placed in powder tray already kept in position over the bed. Spread the powder tray already kept in position over the bed. Spread the powder with the help of a powder spreader so as to fill the bodies of the capsules uniformly. Collect excess of the powder on the platform of the powder tray. Lower the pin plate and move it downward so as to press the powder in the bodies. Remove the powder tray and place the caps holding tray in position. Press the caps with the help of plate with rubber top and operate the lever to unlock the cap and body of the capsules. Remove the loading tray and collect the filled capsules in a tray. With 200 hole machine about 5000 capsules can be filled per hour and with 300 hole machine 7500 capsules can be filled per hour.

5.5 Technology for powder formulation

In case of powder dosages the major process operation are mixing / blending and granulation followed by packaging. For formulation of the powder dosages similar technology as in case of tables and capsules are used.

5.6 Packaging techniques for tablets, capsules and powder

For packaging of tablets, capsules and powder the following method are used.

Bottle Packaging: Bottle packing is resorted to the large unit size e.g. say more than 50/100 tablets or capsules per unit pack. Semi –automatic bottle filling machines with conveyer belt and associated work stations of labeling, stoppering, capping and sealing are available and used. Most widely used bottles are glass / plastic bottles.

Strip Packaging: strip packaging may use paper poly, glassine poly or aluminum poly. Glassine poly and aluminum poly offer better product protection against moisture etc. and aluminium poly is substantially used by the industry. The thickness of packing materials varies marginally.

Blister packaging: It has a lid foil of thermo forming PVC, PVC with PVDC and the base of aluminium foil. Blister packaging machines are used for this type of packaging.

Pouch packaging: the powders are invariably packed in paper laminated aluminium foils by using pouch packaging machines.

5.7 Details and specifications of Machinery & Equipments:

1. **Mechanical Sifter, 30" diameter**, GMP Model, MS Body Cladded with SS, all contact parts in SS-304, suitable for shifting of free flowing powders and granules, with discharged chute, screen loading channel with powder holding arrangement.
2. **Powder and Mass Mixer, 250 kg capacity**, GMP Model, all contact parts in SS-304 with 2 mechanical seal ends, dustproof stainless steel cover, tilting and safety device complete with motor gearbox and starter.
3. **Multi Mill,** GMP Model with all contact parts in steel, rotor fitted with 12 blades and 2 scrapers blades.
4. **Granulator**, GMP Model, 50 kg per hour capacity.
5. **Double Cone Blender,** GMP Model, 250 kg capacity with 5 HP motor, stainless steel cladded body.
6. **Tray Drier with 48 trays** double walled body with 9 kw heater, 1 HP motor.
7. **Peristantic Pumps,** HPP 200.
8. **Rotary tablet machine,** 50,000 tablets per hour with double sided outlet, "D" tooling 3 PC torret with contact parts and die table in SS-316 with complete with dyes and punches.
9. **De dusting unit,** Vibro type, GMP Model and adjustable.
10. **Coating machine with SS coating pan, 30" size,** contact parts in SS-316, 2 HP motor, 45 litres capacity with hot air blower.
11. **Tablet Inspection belt.**
12. **Strip packing machine,** GMP model, 2 track with feeding disc, all contact parts in steel.
13. **PP cap sealing machine,** GMP model, motorized.

14. **Pouch filling and sealing machine,** GMP model, automatic, 250 grams capacity.
15. **Single Pan balance,** 200 grams.
16. **IR moisture balance.**
17. **Tablet hardness tester,** Pfizer type.
18. **Disintegration test apparatus.**
19. **Capsule filling machine** with 300 rolls.
20. **Automatic capsule loader machine,** GMP model.
21. **Stainless steel tanks / storage tanks.**

5.8 Process of manufacture and process flowcharts

The project envisages the manufacture of tablets by compression molding, capsules filling by semi automatic machine and packaging the powder formulations. Accordingly, the proposed unit would comprise of three different departments viz tablet production, capsules production and powder formulation departments. In addition to these there would be a packaging and labeling department as well as facilities for storage of raw materials and finished formulations. The unit would also have facilities for quality control of the various products to be manufactured.

5.8.1 Tablet production department

For efficient operation, the tablet production department shall be divided in to the following three distinct and separate sections.

- Granulating section
- Tableting section
- Coating section.

The following type of machines and equipment would be installed in each of the above three sections.

Granulating section:

- Disintegrator
- Powder mixer
- Mass mixer
- Granulator
- Ovens, thermostatically controlled or other suitable equipment.

Tableting section:

- Tablets machine, single punch or rotary
- Pill machine
- Punch and dies storage cabinet
- Tablet counter
- Tablet inspection belt

- In process testing equipment like hardness, tester, accurate weighing balance and disintegration test apparatus.

Coating section

- Jacketed kittle, steam gas or electricity heated for preparing solution.
- Coating pan
- Polishing pan
- Heater and exhaust system
- Air conditioning and dehumidification arrangement.

The coating section shall be made dust free and suitable exhaust arrangement shall be provided to remove excess powder and the fumes resulting from evaporation of solvent.

5.8.2 Capsule production department

The capsule production unit shall mainly comprise of the following two sections:

- Drug formulation section
- Capsule filling section

Drug formulation section

The main operation involved in drug formulation for capsule includes mixing and blending. In view of the small quantum of production of capsules, it is recommended that the machines and equipment in the granulation unit for the tablets would be used for formulation of drug batches for capsule filling also.

Capsules filling section:

The unit shall have the facility for filling of hard gelatin capsules and the following machines and equipment would be required.

- Semi automatic capsule filling machine
- Capsule counters

5.9 Powder formulation departments

Certain products like ORS and chlorine powder are required to be formulated and packed in paper aluminium laminate sachets. As the basic operation involved in the manufacture of powder formulations is mixing / blending and the requirement level is of relatively lower magnitude, the facilities installed in the granulation section of tablet department shall be used for formulation of powder also.

5.10 Packaging section for tablets, capsules and powder

Keeping in view the facts that Ministry of Health, Govt. of Bhutan would be major buyer for tablets and capsules and the supplies are mainly in the form of bulk packages of 100 to 1000 numbers of tablets or capsules, the packaging unit shall have facility for bulk packaging of these products in bottles. Further, some quantity of these formulations would be required in the form of strip packaging and blister packaging mainly for supply to medical stores and the unit shall also have the facility for the same. The powders are required to be packed in sachets and a machine for sachet packaging shall also be installed in the packaging section. Accordingly, the following machine would be required in the packaging section.

- Bottle packaging and sealing machine.
- Blister packaging machine
- Strip packaging machine.
- Sachet packaging machine
- Foil printing machine

5.11 Process Technologies used

As would be seen from the above, various types of technologies and machines are used for manufacturing tablets and capsules. Similarly, various types of techniques are used for packaging of these products. The main commercial technologies being used have been described earlier. These mainly include various types of tablets making technologies and machines. In the project, a rotary tablet making machine with medium capacity has been recommended. In case of capsules, the capsule filling machines of varying capacities are used. Similarly, different types of packaging techniques viz bulk packaging, strip packaging, blister packaging, foil packaging, etc are used.

5.12 Factors influencing the choice of technology

A number of factors need to be taken into considerations while deciding the choice in favour of a process technology. These factors mainly include the following.

- Advantages of factor inputs
- Market findings viz size of market and recurrence of repeat demand
- Purchasing power of consumers and prevailing price spectrum
- Future projections of market demand
- Availability of skilled manpower and support facilities
- Availability of infrastructure and transport facilities
- Environmental considerations

5.1.3 Technology recommended

A review of the above factors reveals that the market demand for tablet and capsules is relatively of low volume in Bhutan and the Ministry of Health, Government of Bhutan happens to be the main buyer for these products. Besides Government of Bhutan, private medical stores also purchase the tablets and capsules for counter sales. In case of government, the majority of tablets and capsules are purchase in bulk packaging while in case of medical stores, the products are in the form of strip packaging. Accordingly, the project has been based on a medium capacity rotary tablet machine along with coating machine. In case of capsules, a small capacity capsule filling machine has been recommended with automatic loader. A provision has also been made for strip packaging machine in order to cater the requirement of medical stores.

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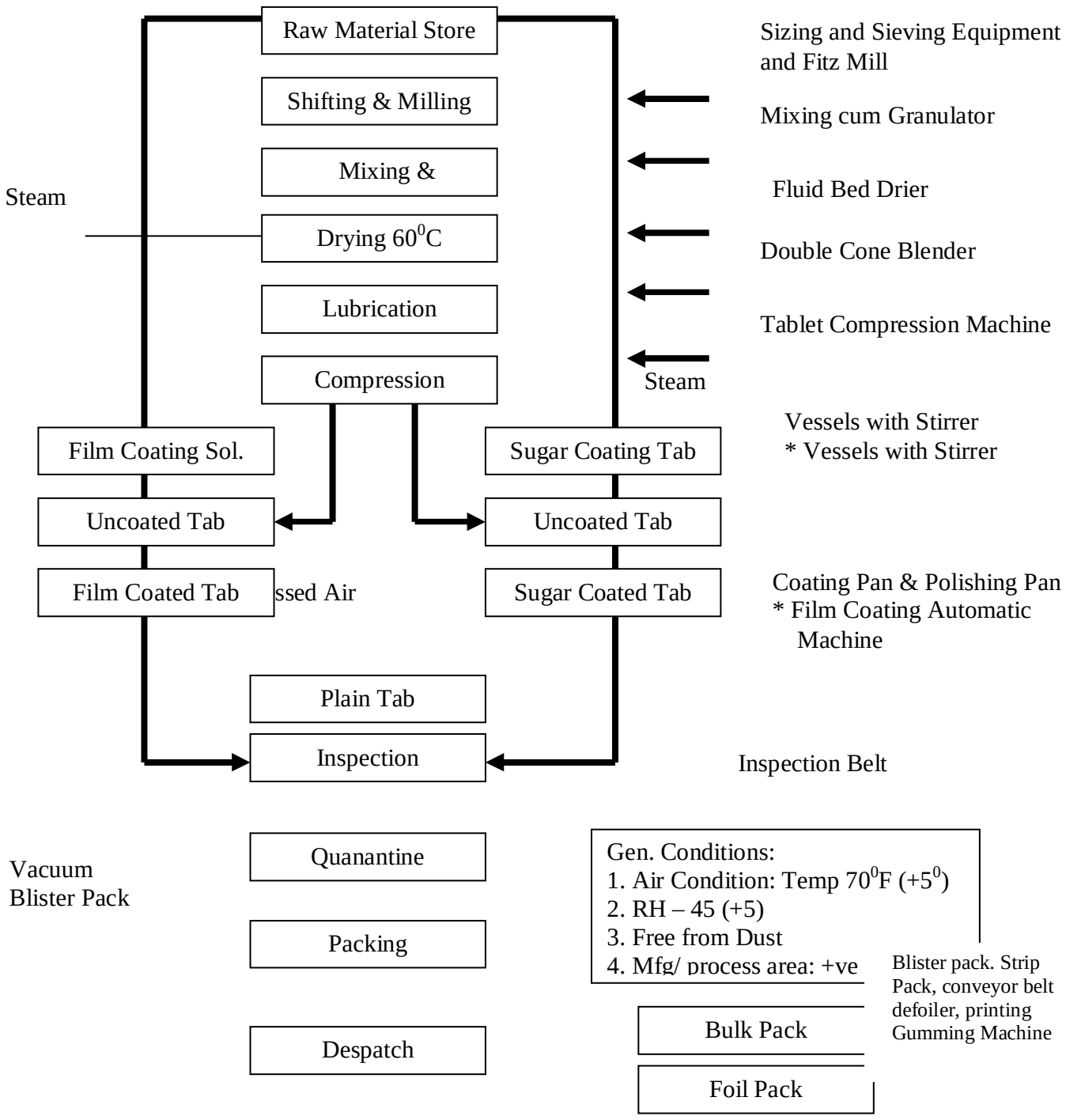
Process Flow Chart for Formulation of Tablet



5.11 Production capacity

The installed capacity of production in tablet section is 1500 lac tablets per annum and in capsule section, the capacity is 125 lac capsules per annum on single shift basis. The production capacity has been calculated on single shift working with 300 days in a year and 80% utilization of installed capacity. Accordingly, the annual production capacity would be 1200 lac of tablets and 100 lacs of capsules per annum.

5.12 Technical know-how

The drug formulation in tablet and capsule form need to be manufacture as per IP, BP and USP specification and in compliance to the standards prescribed by Ministry of Health, Government of Bhutan. The services of manufacturing chemist having sufficient experience in the production of drug formulation would be an essential prerequisite for implementation of the project. Similarly, the services of production supervisors and quality control personnel may also be needed in order to produce quality pharmaceuticals. The machine manufacturers also provide training in their factory as well as on site in proper and efficient operations of their machines.

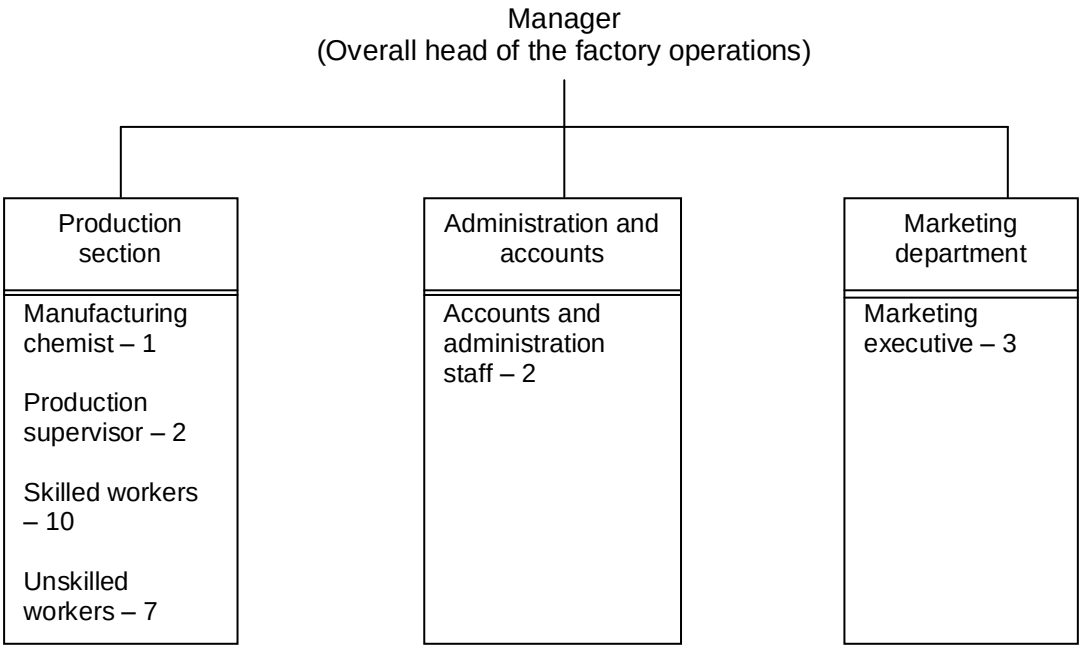
5.13 Requirement of power and fuel

It is estimated that 72 KWH power connection would be required for the production unit including the power requirement for production machines and general purpose lighting. The cost of the power has been calculated on the basis of Re. 1.45 per unit.

5.14 Manpower requirement

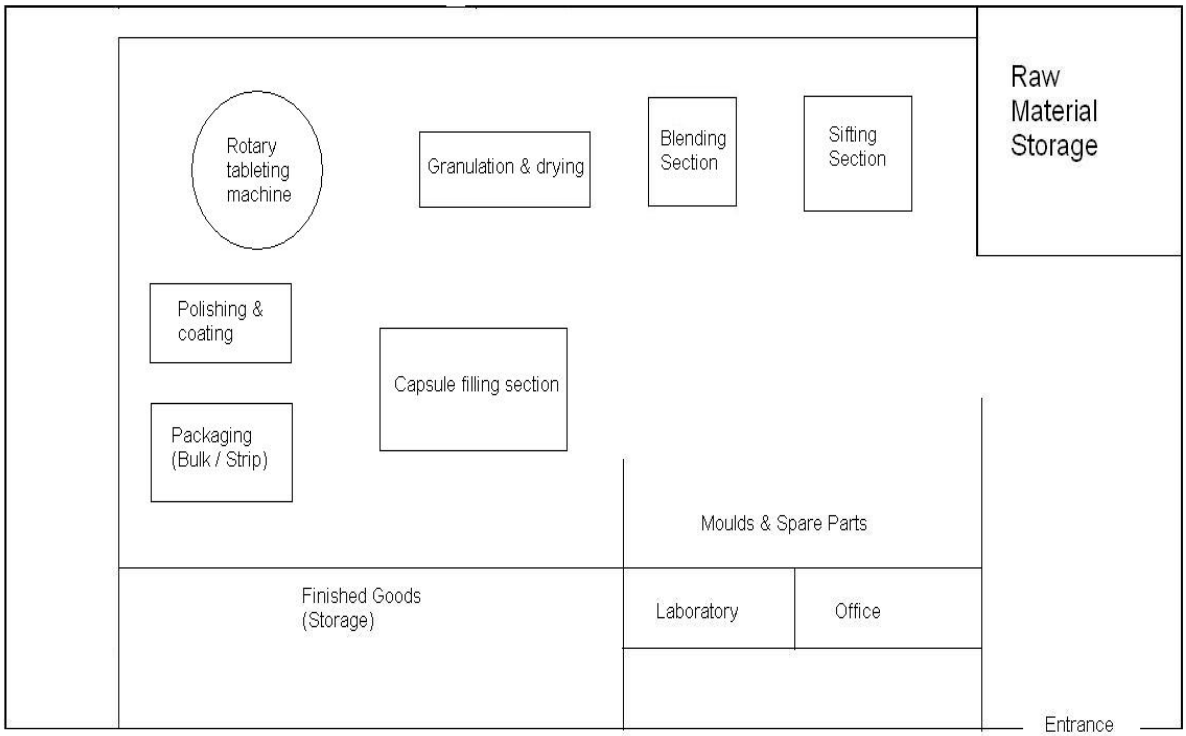
The annual production turnover and the financial projections are based on single shift operation of machines. For operation of the unit, 3 managerial and office staff, 3 marketing executives, 1 manufacturing chemist, 2 production supervisors, 10 skilled workers and 7 unskilled workers would be required. In case the unit is required to be operated in more than one shift, additional staff would be required. In addition to this, there would be a requirement of contract workers during the construction phase of the factory and installation of machinery and equipment. The organization chart for single shift operation would be as under:

5.15 Organization chart



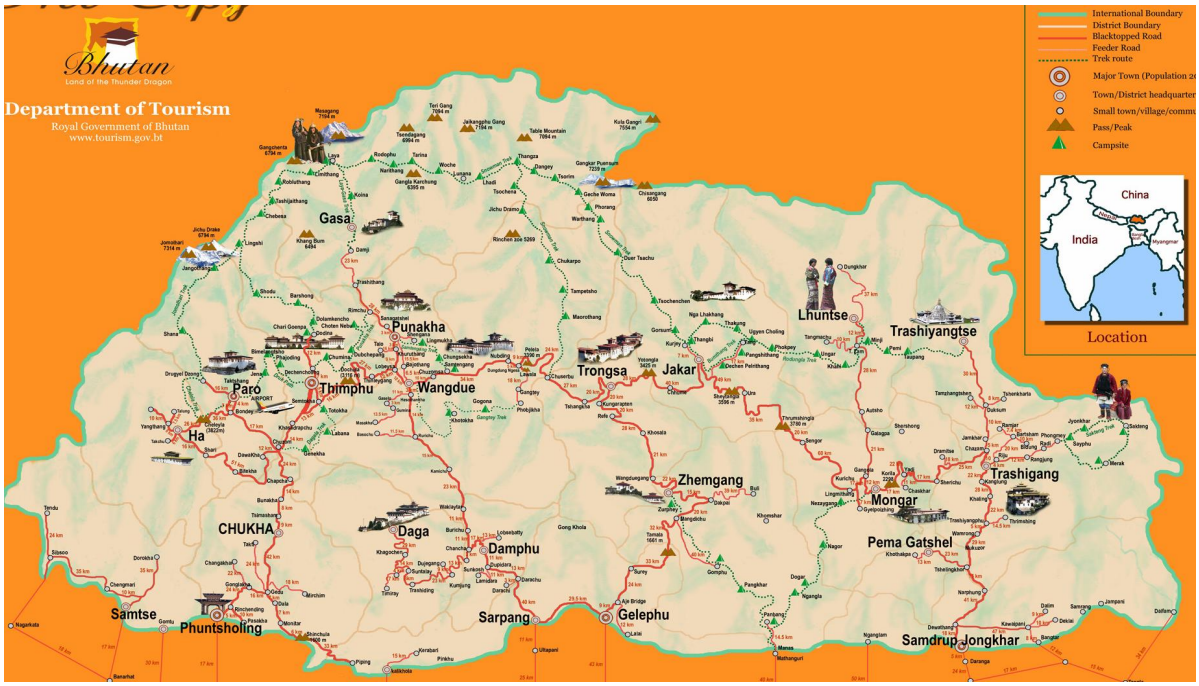
The project has a good employment potential for skilled and unskilled workers which would be employed in the production unit. Beside the project would generate employment potential in marketing & sales of its produce, transport of raw materials and finished products. The project would thus create opportunity both for direct & indirect employment.

5.16 Plant Layout



CHAPTER 6 – PLANT LOCATION AND INFRASTRUCTURE

The consumption of pharmaceuticals formulations particularly the general type of medicines proposed to be manufacture by the unit, to a very large extent is directly related to the population. It would therefore be advisable to setup the formulation unit near to the concentration centres of the population with health care infrastructure. Thimphu, Phuentsholing, Punakha, Gelephu, Samdrup and Paro being the major towns have potential for a drug formulation unit. However, keeping in view that at present, almost the entire supplies of drug formulations in Bhutan are procured by the government and this important aspect has to be kept in view while selecting the location of the unit.



In order to select the suitable location for the manufacturing plant, various parameters viz availability of land, environmental conditions, investments considerations, operational logistics, future development possibilities, socio-economic factors including availability of services like transport facilities etc. have been taken into consideration for ranking the locations. The table below shows the ranking of locations:

Ranking of possible locations based on various parameters

		Weightage of location related parameters						
S. No	Locations	Land access condition	Environmental Conditions	Investment Consideration	Socio economic factors	Operational Logistics	Future development possibilities	Overall Rating
1	Thimphu	7	7	8	8	9	9	**48**
2	Phuentsholing	7	7	7	7	7	5	**40**
3	Paro	7	7	7	4	7	5	37
4	Punakha	7	7	5	6	5	5	35
5	Gelephu	7	7	5	5	5	5	34
6	Samdrup	7	7	5	4	5	5	33

It is therefore proposed that the unit be located at Bjemina Industrial Estate near Thimphu. The requisite infrastructure viz land, power, road transport and communication facilities required for the proposed unit are available in and around Thimphu specially in Bjemina Industrial Estate. The project has been conceptualized in totality and all the manufacturing operations are proposed to be carried out in the unit itself. The project has an inbuilt provision for spare parts, components and tools and the cost for the same has been incorporated. There may be some requirement of minor mechanical or electric repairs which could be taken care of by the skilled workers of the unit. Alternatively, the assistance could be taken of from the existing mechanical and electrical repair workshops. The provision has also been made in the project for a quality control laboratory in order to carry out routine test for tablets and capsules. For specialized testing requirements, the assistance could be taken from the proposed drug testing laboratory at Thimphu or the testing services could be outsourced from India.

In Bhutan, almost entire requirement of medicines is being procured centrally by the government for distribution to various hospitals and basic health units. There are some medical stores which are also selling medicines, however, the quantum of sales in much smaller. As such, the Ministry of Health, Government of Bhutan would be the major purchaser of tablets, capsules and powders proposed to be manufactured by the unit. It would therefore be preferable if the unit is setup near Thimphu vis Bjemina Industrial Estate. It may also be mentioned here that a unit having facilities for production of traditional medicines based tablets and powders is already there in ITMS. The facilities of this unit could be used for training and demonstration to the employees of the proposed unit and estimation of cost of production prior to start of commercial production in the proposed unit. Accordingly, it is recommended that the drug formation unit be preferably setup near Thimphu.

CHAPTER 7 – ENVIRONMENTAL IMPACT

7.1 Environmental aspect of manufacturing process

Pharmaceuticals tablets, capsules and powders are the main products proposed to be manufactured in the unit. For all the three products, the basic drugs and formulation ingredients shall be procured through imports from India and other countries. The process involved in the manufacturing of these formulations broadly includes formulations of basic drugs and ingredients in requisite proportion and then its conversion to tablets or capsules. In case of powders also, the process involves mixing of ingredients and packaging. No liquid formulations are proposed to be manufactured. No solid, liquid or gaseous effluents would be discharged during the manufacturing process and there would be no adverse impact on the environment.

7.2 Waste generated and mitigation measures

The manufacturing process being adopted in the project is environment friendly and no toxic & hazardous waste would be generated. However, there would be some waste of metal scrap, wooden scrap, broken bricks, stone aggregates, etc during construction phase of the project. The waste generated during construction phase is mainly used for earth filling & flooring. The details of the waste generated during construction phase and project operation phase along with mitigation measures are given below in subsequent paras.

7.2.1 Waste generated during construction phase

The details of the waste generated during construction phase and the mitigation measures are as under: -

S. No.	Type of waste / scrap	Quantity	Mitigation measures	Impact on Environment
1.	Metal scrap	Around 2-3 % of the steel used in construction	Sold to trade channels for reprocessing.	No adverse impact
2.	Wooden scrap	Around 5-7% of the wood used in construction.	Used as fuel.	No adverse impact
3.	Clay stones, mounds	Depending upon on the topography of the construction site.	Used for earth filling.	No adverse impact.
4.	Brick stone cement aggregate	5% of the quantity used	Used for flooring and earth filling.	No adverse impact

7.2.2 Waste generated during operation phase

The details of the waste generated and the mitigation measures are as under:

S. No.	Type of waste	Quantity	Mitigation measures	Impact on environment
1.	Liquid effluents	Nil	Not applicable	No adverse impact
2.	Gaseous effluents	Nil	Not applicable	No adverse impact
3.	Floor sweepings powder, broken tablets / capsules, foil cutting and scrap.	1-2% of the raw material used.	Disposal as a normal garbage	No adverse impact

CHAPTER 8 – IMPLEMENTATION SCHEDULE

8.1 Implementation schedule – Table

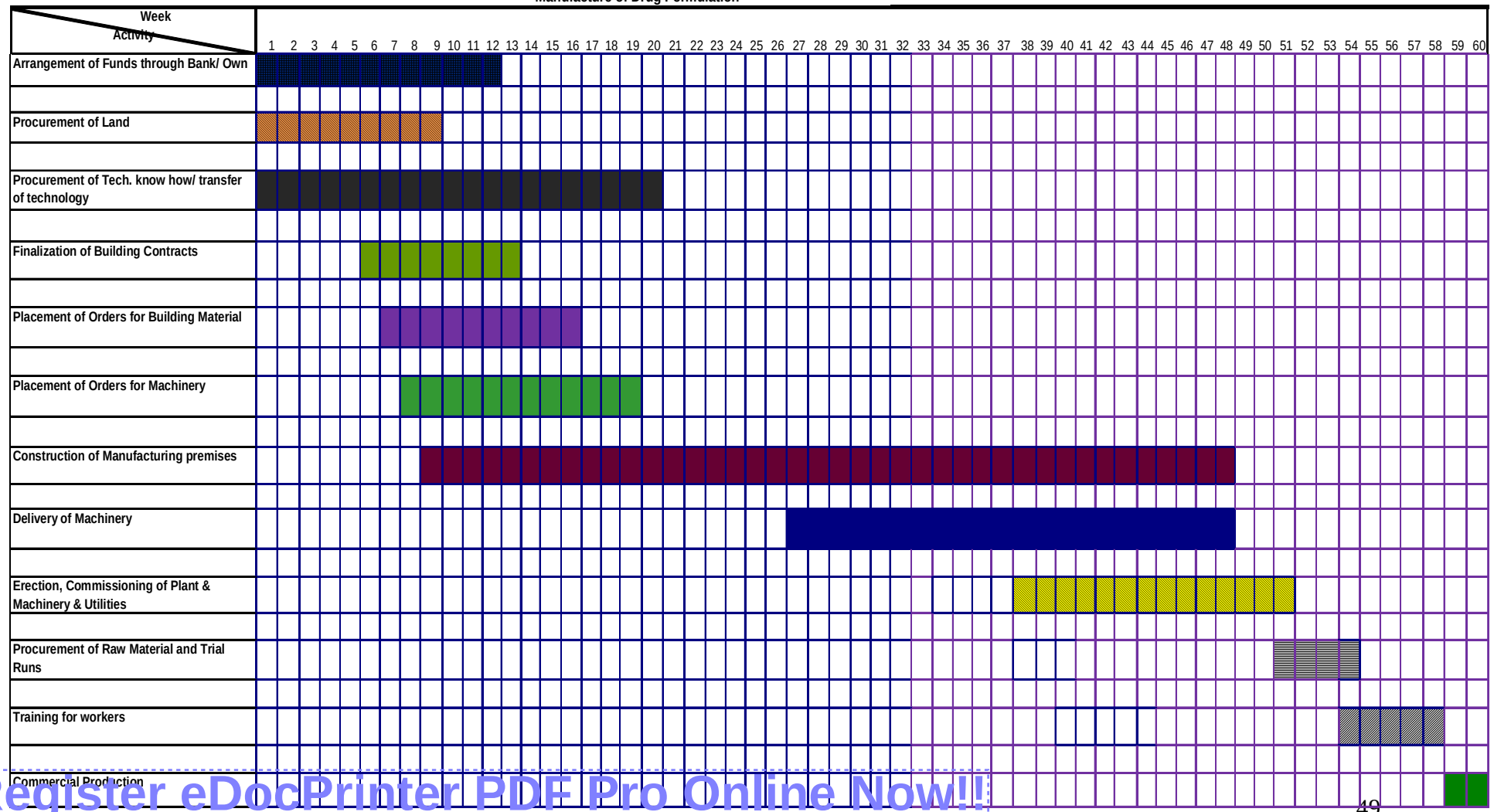
Implementation Schedule for manufacture of Drug Formulation

Particular	From	To	Total Weeks
Arrangement of Funds through Bank/ Own	1	12	12
Procurement of Land	1	9	9
Procurement of Tech. know how/ transfer of technology	1	20	20
Finalization of Building Contracts	6	12	6
Placement of Orders for Building Material	7	16	9
Placement of Orders for Machinery	8	19	11
Construction of Manufacturing premises	9	47	38
Delivery of Machinery	27	48	21
Erection, Commissioning of Plant & Machinery & Utilities	38	51	13
Procurement of Raw Material and Trial Runs	51	54	3
Training for workers	54	58	4
Commercial Production	59	60	1

8.2 Implementation schedule – Graphic View

Implementation Schedule

Manufacture of Drug Formulation



CHAPTER 9 – COST PRESENTATION

9.1 Capital Cost

9.1.1 Cost of land and building

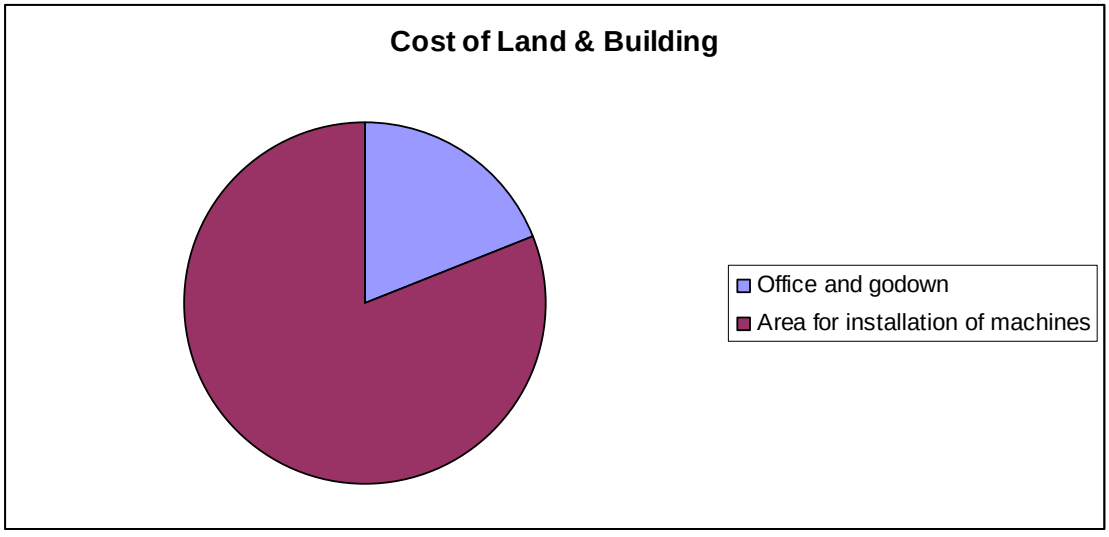
A). Plot and built up area

- Total land requirement	-	1000 sq. mt.
- Constructed area for godowns and offices	-	150 sq. mt.
- Constructed are for installation of production sections packaging section & laboratory	-	650 sq. mt

B). Cost of construction

-Office and godown (150 X 6000)	-	Rs. 9,00,000/-
- Built up area for machine installation (650 X 6000)	-	Rs. 39,00,000/-
Total cost of construction	**-**	**Rs. 48,00,000/-**

C). Land on lease @ Rs. 10/- per sq mt / annum



9.1.2 Cost of machinery & equipments

1. Mechanical Sifter, 30” diameter	-	Rs. 1,00,000/-
2. Powder and Mass Mixer, 250 kg capacity	-	Rs. 2,96,000/-
3. Multi Mill	-	Rs. 90,000/-
4. Granulator	-	Rs. 60,000/-
5. Double Cone Blender	-	Rs. 2,50,000/-

6. Tray Drier with 48 trays	-	Rs. 1,80,000/-
7. Peristantic Pumps	-	Rs. 50,000/-
8. Rotary tablet machine	-	Rs. 12,00,000/-
9. De dusting unit	-	Rs. 55,000/-
10. Coating machine with SS coating pan, 30" size	-	Rs. 2,90,000/-
11. Tablet inspection belt	-	Rs. 1,10,000/-
12. Strip packing machine	-	Rs. 1,80,000/-
13. PP cap sealing machine	-	Rs. 45,000/-
14. Pouch filling and sealing machine	-	Rs. 1,55,000/-
15. Single Pan balance	-	Rs. 10,000/-
16. IR moisture balance	-	Rs. 8,500/-
17. Tablet hardness tester	-	Rs. 7,000/-
18. Disintegration test apparatus	-	Rs. 24,000/-
19. Capsule filling machine	-	Rs. 75,000/-
20. Automatic capsule loader machine	-	Rs. 1,30,000/-
21. Stainless steel tanks / storage tanks	-	Rs. 2,50,000/-
Total	**-**	**Rs. 35,65,500/-**

9.1.3 Miscellaneous fixed assets - Rs. 2,00,000

9.2 Operating cost

9.2.1 Cost of raw materials

A). Paracetamol tablets:

Raw materials for 1,00,000 tablets

• Paracetamol tablets 50 kg @ Rs. 250 per kg	-	Rs. 12,500/-
• Stearie Acid 4 kg @ Rs. 25 per kg	-	Rs. 100/-
• MCCP 2 kg @ Rs. 60 per kg	-	Rs. 120/-
• Other formulations ingredients viz talc, starch, MP, PP, Mg stearate.	-	Rs. 800/-
• Packing cost – lose in bottles	-	Rs. 480/-
Sub-total	**-**	**Rs. 14,000/-**
Total raw material cost for 400 lacs tablets	-	Rs. 56,00,000/-

B). Anta acid tablet:

Raw material for 1,00,000 tablets

• Aluminium Hydroxide 25 kg @ Rs. 120 per kg	-	Rs. 3,000/-
• Magnesium Hydroxide 25 kg @ Rs. 80 per kg	-	Rs. 2,000/-
• Symithine 2.5 kg @ Rs. 30 per kg	-	Rs. 70/-
• Packing cost – lose in bottles	-	Rs. 480/-
Sub-Total	**-**	**Rs. 5,550/-**
Raw material for 400 lac tablets	–	Rs 22,20,000/-

C). Iron folic acid tablets:

Raw materials for 1,00,000 tablets

- Ferrous sulphate 15 kg @ Rs. 30/- per kg - Rs. 450/-
- Folic acid 0.75 kg @ Rs. 300/- per kg - Rs. 225/-
- Other formulation ingredients - Rs. 325/-
- Tablet Coating cost - Rs. 3,000/-

Sub-total - **Rs. 4,000/-**

Raw materials for 400 lac tablets – Rs. 16,00,000/-

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D). B-Complex capsules

Raw materials for 1,00,000 capsules

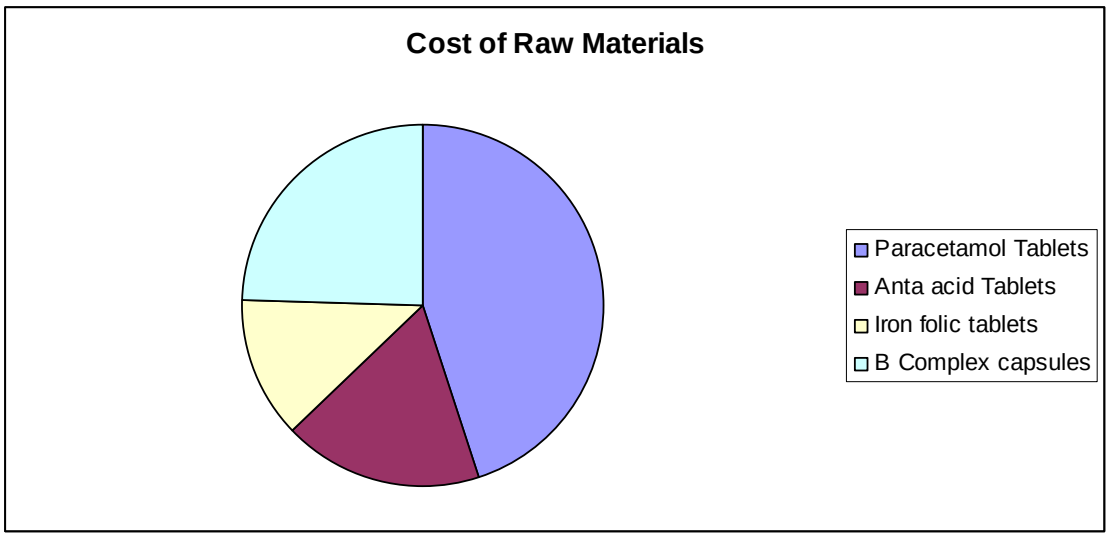
Cost of 1,00,000 capsules shells @ Re. 0.1 per shell = Rs. 10,000/-

- B1, B6, B12 raw materials = Rs. 12,000/-
- Minerals = Rs. 4,500/-
- Packaging material = Rs. 4,000/-

Sub-total **= Rs. 30,500/-**

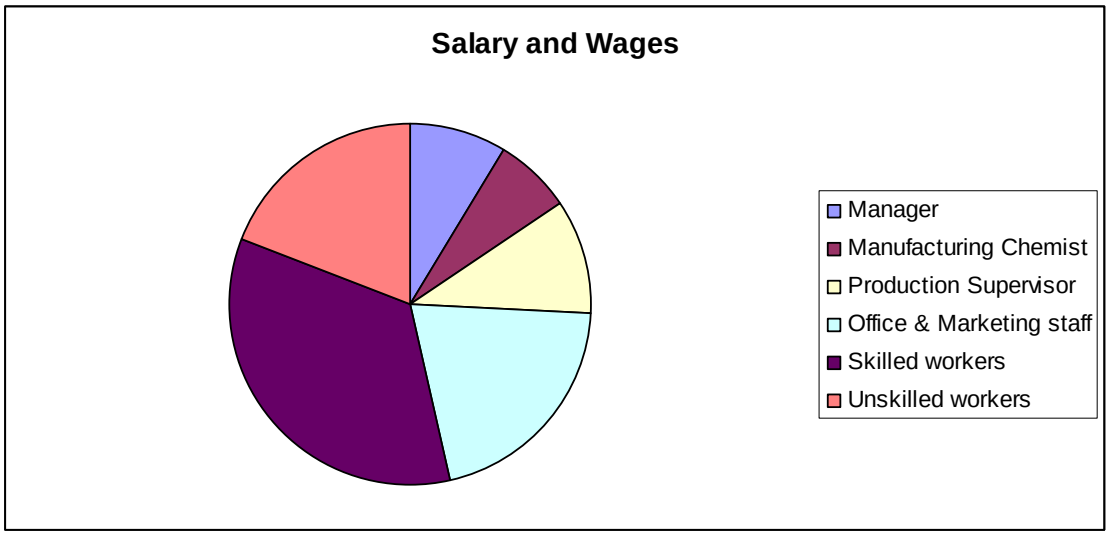
Raw material cost for 1,00,00,000 capsules = Rs. 30,50,000/-

E). Total raw materials cost = Rs. 1,24,70,000/-



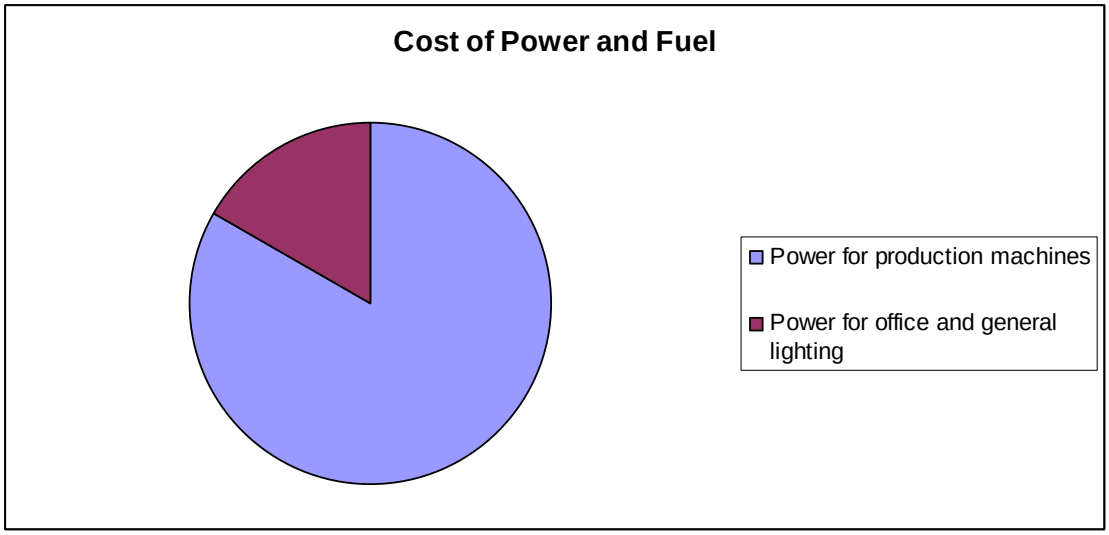
9.2.2 Salary and wages

Manager	-	1 no	-	Rs. 25,000/-
Manufacturing chemist	-	1 no	-	Rs. 20,000/-
Production supervisor	-	2 nos	-	Rs. 30,000/-
Office staff & marketing executive	-	5 nos	-	Rs. 60,000/-
Skilled workers	-	10 nos	-	Rs. 1,00,000/-
Unskilled workers	-	7 nos	-	Rs. 56,000/-
Total			**-**	**Rs. 2,91,000/-**
Total salary and wages (per annum)			-	Rs. 34,92,000/-



9.2.3 Cost of power and fuel

Power requirement for production machines	-	60 KWH
Power requirement for general purpose with lighting Of stores, offices and production unit	-	12 KWH
Total	**-**	**72 KWH**



9.2.4 Annual turnover

1. Paracetamol tablet – 400 lacs @ Re. 0.18 = Rs. 72,00,000/-
2. Anta Acid tablet – 400 lacs @ Re. 0.08 = Rs. 32,00,000/-
3. Iron Folic Acid – 400 lacs @ Re. 0.08 = Rs. 32,00,000/-
4. B-Complex Capsules – 100 lacs @ Re. 0.5 = Rs. 50,00,000/-

Total = Rs. 1,86,00,000/-

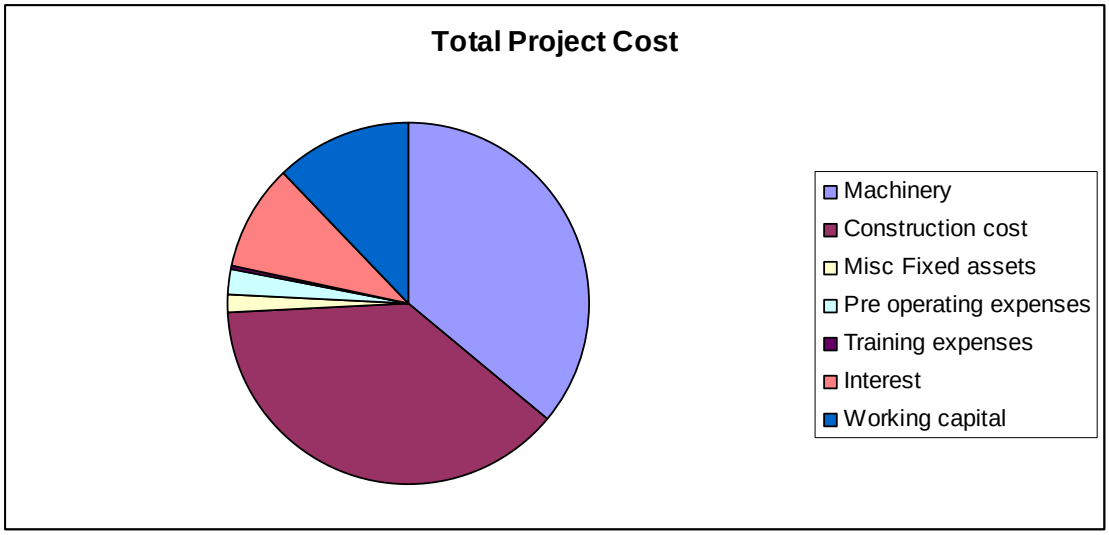
CHAPTER 10 – FINANCIAL ANALYSIS

10.1 Project Assumptions

Assumptions at a Glance		
S. No.	**Particulars**	**Rate/Amount**
1	Total Project Cost	126.03
2	Debt	70%
3	Equity	30%
4	Rate of Interest	12%
5	Depreciation (Building)	SLM 10 yrs
6	Depreciation (Machinery)	SLM 20 yrs
7	Tax	30%
8	Construction Cost (Building) per sq.m.	6000
9	Construction Cost (Shed) per sq.m.	3500
10	Repayment period of Debt	8 yrs
11	Moratorium period	1 yr.
12	Installed Capacity (Units in lacs)	1625
13	Capacity Utilization	90%
14	Working Capital Cycle	1 month

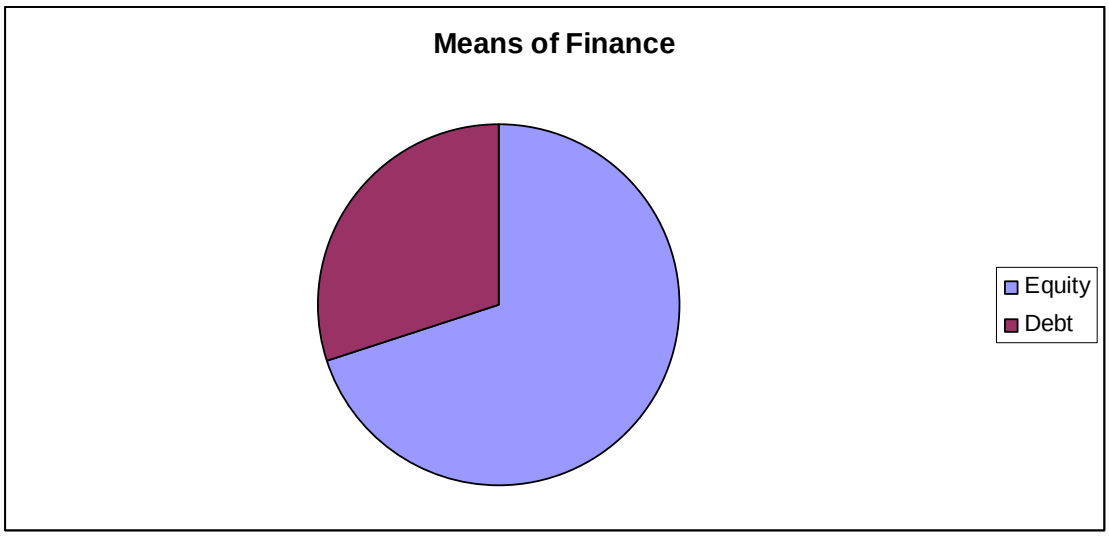
10.2 Total project cost

Total project cost (Rs. In lacs)		
1	Machinery	45.40
2	Construction cost	48.00
3	Miscellaneous fixed assets	2.00
4	Pre operating expenses	3.00
5	Training expense	0.45
6	Interest	11.86
7	Working capital	15.32
	Total	**126.03**



10.3 Means of finance

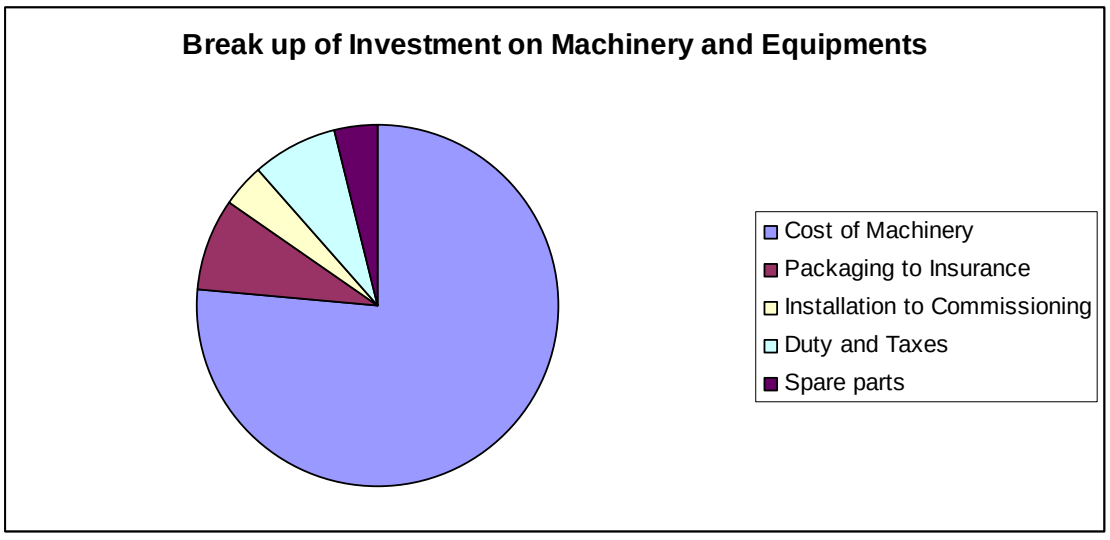
Means of finance		
	Rs. in lacs	
Debt	88.22	70%
Equity	37.81	30%
Total	**126.03**	**100%**



10.4 Investment on machinery and equipments

TOTAL INVESTMENT ON MACHINERY & EQUIPMENT

	M1	100,000
	M2	296,000
	M3	90,000
	M4	60,000
	M5	250,000
	M6	180,000
	M7	50,000
	M8	1,200,000
	M9	55,000
	M10	290,000
	M11	110,000
	M12	180,000
	M13	45,000
	M14	155,000
	M15	10,000
	M16	8,500
	M17	7,000
	M18	24,000
	M19	75,000
	M20	130,000
	M21	250,000
	Total	**3,465,500**
Add	Packaging, forwarding, transport and insurance @ 11%	381205
Add	Installation, erection and commissioning @ 5%	173275
Add	Duty and taxes @ 10%	346550
Add	Spare parts @ 5%	173275
	Total cost	**4,539,805**

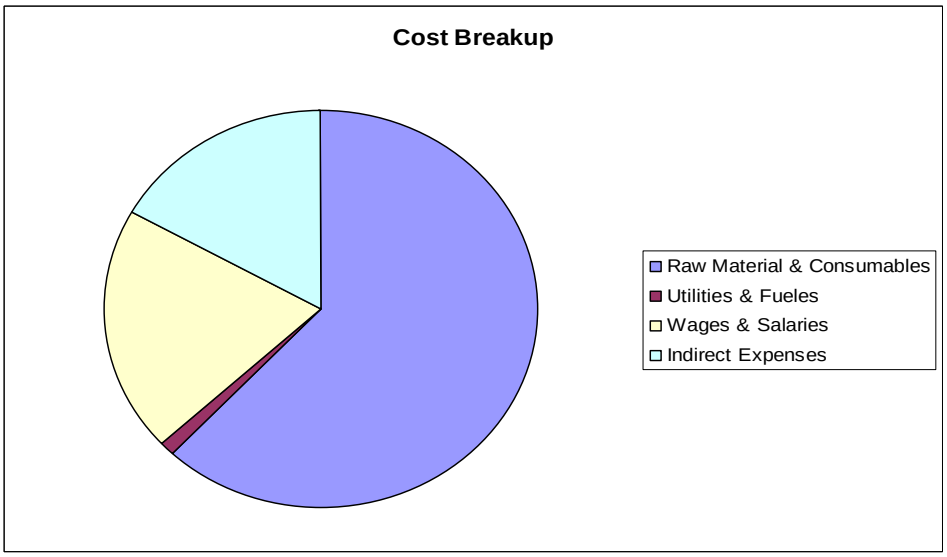


10.5 Cost of construction

Construction cost	Amount
Constructed area (800 Sq. mtr @ 6000 per sq mts)	4800000
Shed (00 sq mt @ 3500 per sq mt)	
Total	**4800000**

10.6 Cost break up

Particulars	Amount (In lacs)
Raw material & consumables	124.70
Utilities & fuels	2.48
Wages & salaries	40.16
Indirect expenses	34.03



10.7 Expenses incurred

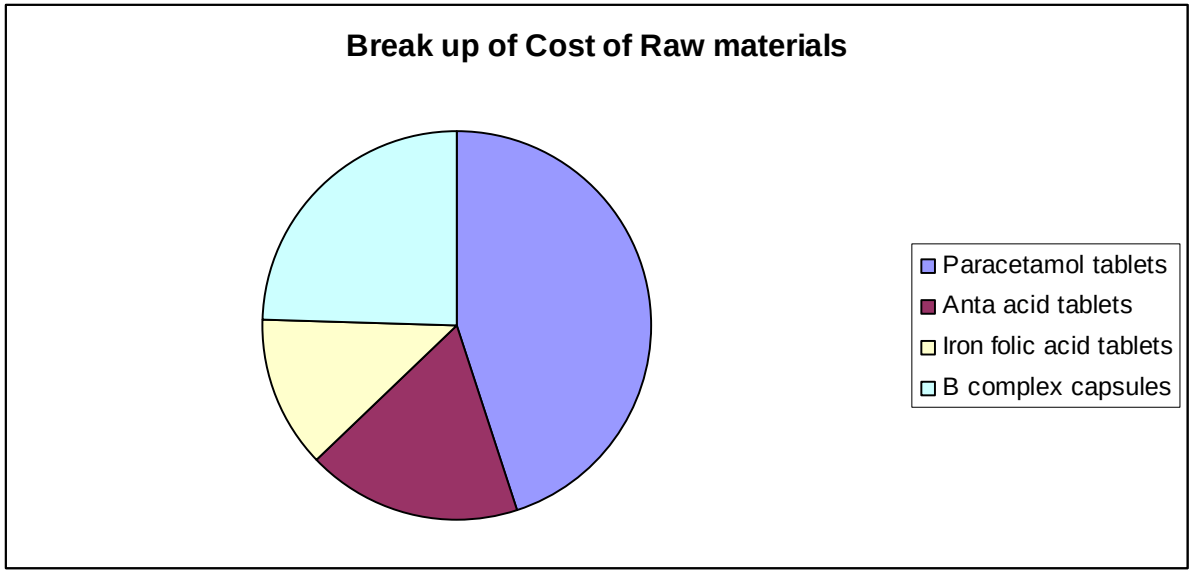
Expenses (in Rs.)

1	Salary and Wages				
	Type of Employees	No. of Employees	Per month	Per Annum	Total
	Manager	1	25000	300000	3
	Manufacturing Chemist	1	20000	240000	2.4
	Production Supervisor	2	15000	180000	3.6
	Office's Staffs and Marketing Executive	5	12000	144000	7.2
	Skilled Workers	10	10000	120000	12
	Unskilled Workers	7	8000	96000	6.72
	Total				**34.92**
	Perks		at 15%		5.24
	Total				**40.16**
2	Training and Development Cost (1% of Machinery)				0.45
3	Power (90HP @ .75per hour,80% utilisation, 8hrs/day,25days/month)	Rate=1.45/unit	15660		1.88
4	Diesel, Water		5000		0.6
5	Selling Expenses (Publicity and Marketing Expense)	5% of Sales			11.4
	Total				**19.57**

10.8 Cost of raw materials

Raw Material Cost (Per Unit)

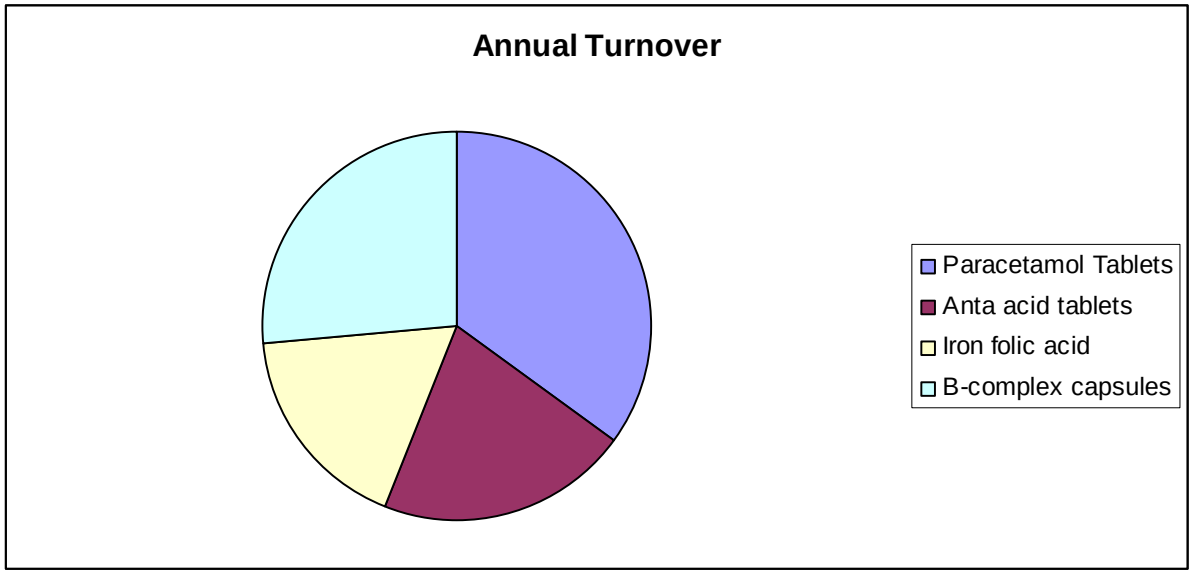
Particulars	Amount
A) Paracetamol Tablets	
	5,000,000
	40,000
	48,000
	320,000
	192,000
Sub Total	**5,600,000**
B) Anta acid tablets	
	1,200,000
	800,000
	28,000
	192,000
Sub Total	**2,220,000**
C) Iron folic acid tablets	
	180,000
	90,000
	130,000
	1,200,000
Sub Total	**1,600,000**
D) **B-Complex capsules**	
	1,000,000
	1,200,000
	450,000
	400,000
Sub Total	**3,050,000**
Total	**12,470,000**



10.9 Annual turnover

Turnover

Particulars	Units in lacs	Rate	Total
Paracetamol Tablets	400	20000	8000000
Anta acid tablets	400	12000	4800000
Iron folic acid	400	10000	4000000
B-complex capsules	100	60000	6000000
Total	**1,300**		**22,800,000**



10.10 Income statement

Income Statement

Operating years		1	2	3	4	5	6	7	8	9	10
Capacity											
Installed Capacity (In Lakhs)		1625.00	1625.00	1625.00	1625.00	1625.00	1625.00	1625.00	1625.00	1625.00	1625.00
Capacity Utilisation		80%	80%	80%	80%	80%	80%	80%	80%	80%	80%
PRODUCTION		1300	1300	1300	1300	1300	1300	1300	1300	1300	1300
Sales Revenue		228.00	228.00	228.00	228.00	228.00	228.00	228.00	228.00	228.00	228.00
Raw Material & Consumables		124.70	124.70	124.70	124.70	124.70	124.70	124.70	124.70	124.70	124.70
Utilities & Fueles											
Power		1.88	1.88	1.88	1.88	1.88	1.88	1.88	1.88	1.88	1.88
Water, Diesel, etc		0.60	0.60	0.60	0.60	0.60	0.60	0.60	0.60	0.60	0.60
Sub Total		2.48	2.48	2.48	2.48	2.48	2.48	2.48	2.48	2.48	2.48
Wages & Salaries		40.16	40.16	40.16	40.16	40.16	40.16	40.16	40.16	40.16	40.16
Factory Overheads		3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00	3.00
General Overheads		2.00	2.00	2.00	2.00	2.00	2.00	2.00	2.00	2.00	2.00
Lease											
Land		0.10	0.10	0.10	0.10	0.10	0.10	0.10	0.10	0.10	0.10
Estimated Cost of Production		172.44	172.44	172.44	172.44	172.44	172.44	172.44	172.44	172.44	172.44
Selling Expenses		11.40	11.40	11.40	11.40	11.40	11.40	11.40	11.40	11.40	11.40
Cost of Sales		183.84	183.84	183.84	183.84	183.84	183.84	183.84	183.84	183.84	183.84
EBITDA		44.16	44.16	44.16	44.16	44.16	44.16	44.16	44.16	44.16	44.16
Interest		10.59	9.26	7.94	6.62	5.29	3.97	2.65	1.32	0.00	0.00
Depreciation		6.94	6.94	6.94	6.94	6.94	6.94	6.94	6.94	6.94	6.94
PBT		26.64	27.96	29.28	30.61	31.93	33.25	34.58	35.90	37.22	37.22
Taxation		7.99	8.39	8.78	9.18	9.58	9.98	10.37	10.77	11.17	11.17
PAT		18.65	19.57	20.50	21.42	22.35	23.28	24.20	25.13	26.06	26.06

It would be seen from table above that the PBT in the 1st year of operation in Rs. 26.64 lacs which works out to be 12% of the total sales. In the 10th year, the %age of PBT would be 16%. Similarly PAT in the 1st year is Rs. 18.65 lacs accounting for 8% of total turnover. PAT in 10th would rise to 11%. These figures could vary depending upon change in tax structure.

10.11 Repayment of interest schedule

Repayment and Interest Schedule for Loans

									126.03	88.22	11.02798
Operating Years	1	2	3	4	5	6	7	8	9	10	
Rate of Interest	12%										
Loan (Outstanding)	88.22	77.20	66.17	55.14	44.11	33.08	22.06	11.03	0.00	0.00	
Interest	10.59	9.26	7.94	6.62	5.29	3.97	2.65	1.32	0.00	0.00	
Moratorium											
Repayment	11.03	11.03	11.03	11.03	11.03	11.03	11.03	11.03	0.00	0.00	
Closing Balance	77.20	66.17	55.14	44.11	33.08	22.06	11.03	0.00	0.00	0.00	

10.12 Depreciation

Depreciation

Operating Years		1	2	3	4	5	6	7	8	9	10
Machinery @ 10%		4.54	4.54	4.54	4.54	4.54	4.54	4.54	4.54	4.54	4.54
Construction Cost @ 5%		2.40	2.40	2.40	2.40	2.40	2.40	2.40	2.40	2.40	2.40
Total		**6.94**	**6.94**	**6.94**	**6.94**	**6.94**	**6.94**	**6.94**	**6.94**	**6.94**	**6.94**

10.13 Projected fund flow statement

Projected Funds Flow Statement

Sn		Construction Period	Operation period									
	Years	1	1	2	3	4	5	6	7	8	9	10
	SOURCES OF FUNDS											
	Equity	37.81										
	Debt	88.22										
	PBDIT		44.16	44.16	44.16	44.16	44.16	44.16	44.16	44.16	44.16	44.16
	Total Sources A	126.03	44.16	44.16	44.16	44.16	44.16	44.16	44.16	44.16	44.16	44.16
	APPLICATION OF FUNDS											
	Fixed Assets Purchase	108.71										
	Miscellaneous Fixed Assets	2.00										
	Increase in Current Assets	15.32										
	Repayment of Loan Payment		11.03	11.03	11.03	11.03	11.03	11.03	11.03	11.03	0.00	0.00
	Payment of Interest on Term Loan		10.59	9.26	7.94	6.62	5.29	3.97	2.65	1.32	0.00	0.00
	Taxation		7.99	8.39	8.78	9.18	9.58	9.98	10.37	10.77	11.17	11.17
	Total Application B	126.03	29.61	28.68	27.75	26.83	25.90	24.97	24.05	23.12	11.17	11.17
	SURPLUS/(DEFICIT) A-B	0.00	14.56	15.48	16.41	17.34	18.26	19.19	20.12	21.04	33.00	33.00
	OPENING CASH & BANK BALANCES		0.00	14.56	30.04	46.45	63.79	82.05	101.24	121.35	142.39	175.39
	CLOSING CASH & BANK BALANCES	0.00	14.56	30.04	46.45	63.79	82.05	101.24	121.35	142.39	175.39	208.39

10.14 Projected balance sheet

	Projected Balance Sheet											
Sn	**Description**	**Construction Period**	**Operati0on Period**									
		1	1	2	3	4	5	6	7	8	9	10
1.1	Equity	37.81	37.81	37.81	37.81	37.81	37.81	37.81	37.81	37.81	37.81	37.81
1.2	General Reserves		18.65	38.22	58.71	80.14	102.49	125.77	149.97	175.10	201.16	227.21
1.3	Debt	88.22	77.20	66.17	55.14	44.11	33.08	22.06	11.03	0.00	0.00	0.00
	Total Liabilities	**126.03**	**133.65**	**142.20**	**151.67**	**162.06**	**173.38**	**185.63**	**198.81**	**212.91**	**238.97**	**265.02**
2	**Assets**											
2.1	Gross Fixed Assets	110.71	110.71	110.71	110.71	110.71	110.71	110.71	110.71	110.71	110.71	110.71
2.2	Accumulated Depreciation		6.94	13.88	20.82	27.76	34.70	41.64	48.58	55.52	62.46	69.40
2.3	Net Fixed Assets	110.71	103.77	96.83	89.89	82.96	76.02	69.08	62.14	55.20	48.26	41.32
2.4	Working Capital Assets	15.32	15.32	15.32	15.32	15.32	15.32	15.32	15.32	15.32	15.32	15.32
2.5	Cash & Bank Balances	0	14.56	30.04	46.45	63.79	82.05	101.24	121.35	142.39	175.39	208.39
	Total Assets	**126.03**	**133.65**	**142.20**	**151.67**	**162.06**	**173.38**	**185.63**	**198.81**	**212.91**	**238.97**	**265.02**

10.15 Discounted cash flow statement

	Discounted Cash flow statement (Total Investment)											
	Construction Period		Operation Period									
Years	t=0	t=1	1	2	3	4	5	6	7	8	9	10
Inflows												
Net Cash Accruals After Interest & Tax			25.59	26.51	27.44	28.36	29.29	30.22	31.14	32.07	33.00	33.00
Less: Change in Working Capital			0	0	0	0	0	0	0	0	0	0
Add back financial Expenses			10.59	9.26	7.94	6.62	5.29	3.97	2.65	1.32	0.00	0.00
Terminal value												120
Total inflow			36.17	35.77	35.38	34.98	34.58	34.19	33.79	33.39	33.00	153.00
Outflows												
Investment	110.71	15.32										
Bridge Loan	0	0										
Total outflow	110.71	15.32										
Net Cashflow	-110.71	-15.32	36.17	35.77	35.38	34.98	34.58	34.19	33.79	33.39	33.00	153.00
IRR on Investment (%)	23%											
NPV (12% Discount Rate)	Rs. 76.36											
Pay Back Period	3years 6 months											
	Discounted Cashflow Statement (Equity)											
Years	t=o	t=1	1	2	3	4	5	6	7	8	9	10
Inflows												
Net Cash Accruals After Interest & Tax			25.59	26.51	27.44	28.36	29.29	30.22	31.14	32.07	33.00	33.00
Less: Change in Working Capital			0	0	0	0	0	0	0	0	0	0
Less: Loan Repayment			11.03	11.03	11.03	11.03	11.03	11.03	11.03	11.03	0.00	0.00
Terminal Value												92
Total Inflow			14.56	15.48	16.41	17.34	18.26	19.19	20.12	21.04	33.00	125.00
Outflows												
Equity	33.21	4.60										
Total Outflow	33.21	4.60										
Net Cash Flow	-33.21	-4.60	14.56	15.48	16.41	17.34	18.26	19.19	20.12	21.04	33.00	125.00
IRR on Equity	36%											

The IRR on investment is 23% which is quite a positive indication about the financial health of the project because the cost of borrowing is 12%. Similarly IRR on Equity is 36% which again is a positive indicator. The NPV @ of 12% on investment is Rs. 76.36 lacs which is quite good for any investment.

10.16 Break even point and sensitivity analysis

	Break Even Point And Senstivity Analysis				
	Normal	Case1	Case2	Case3	Case4
Variable Cost (Rs. Lacs)					
Raw material & Consumable Stores	124.70	137.17	124.70	124.70	137.17
Utilities	2.48	2.73	2.48	2.48	2.73
Total Variable Cost	127.18	139.90	127.18	127.18	139.90
Average Variable Cost (Rs. / lacs unit)	9783.02	10761.32	9783.02	9783.02	10761.32
Fixed Cost (Rs. Lacs)					
Wages & Salaries	40.16	40.16	44.17	40.16	42.17
Repairs & Maintenance	3.00	3.00	3.30	3.00	3.15
General Overheads	2.00	2.00	2.20	2.00	2.10
Lease charges	0.10	0.10	0.11	0.10	0.11
Financial Expenses	10.59	10.59	11.65	11.65	12.23
Depreciation	6.94	6.94	7.63	7.63	8.02
Total Fixed Cost (Rs. Lacs)	62.78	62.78	69.06	64.54	67.76
Average Fixed Cost (Rs. per lacs units)	4829.59	4829.59	575.53	537.81	564.70
Average Selling Price	17538.46	17538.46	17538.46	17538.46	16661.54
Project Break Even Point (t)	810	926	891	832	1149
Project Break Even	62%	71%	69%	64%	88%
Cash Break Even Point	720	824	792	734	1013
Cash Break Even	55%	63%	61%	56%	78%

Case 1 - 10% Increase in Variable Cost
Case 2 - 10% Increase in fixed Cost
Case 3 - 10% Increase in Project Cost
Case 4 - 10% Increase in Variable Cost and Fixed Cost
5% Increase in Fixed Cost
5% Dcrease in Selling Price

The project break even in normal case is 55% i.e. after achieving 55% of the Projected Turn Over the unit would be in be in the profit zone

10.17 Ratio analysis

Ratio Analysis		
1	Return on assets	15%
2	Return on equity	49%
3	Debt-equity ratio	2.33%
4	Interest coverage ratio	4

10.18 Foreign exchange implications

The foreign exchange requirement for the project would be only for the import of machines, equipments and accessories for a value of Rs. 36 lacs, during the setting up of the project. Approximately, Rs. 5 lacs worth of foreign exchange would be required for incidental expenses such as training, travel, etc. Additionally, there would be a requirement of Rs. 125 lacs per annum for the import of raw materials. Thus, the foreign exchange expenditures during first five years would be Rs. 670 lacs. The foreign exchange saving in terms of import substitution would be around Rs. 1140 lacs during the first five years of operation of the project.

CHAPTER 11 – ECONOMIC ANALYSIS

11.1 Economic Rate of Return (ERR)

Economic Rate of Return (ERR) is the interest rate at which the cost and benefits of a project, discounted over its life, and equal. ERR differs from Financial Rate of Return in that it takes into account the effects of factors such as price controls, subsidies and tax breaks from local government, to compute the actual cost of the project to the economy.

The economic rate of return also includes indirect benefits to the economy that are likely to be ploughed back to the investors, people, government and other government or non-government agencies, over a longer period of time.

11.2 Relevance of ERR to the project

It may be mentioned that the concept of ERR is more relevant for big projects involving large capital deployment. For small projects like the project on drug formulation, there may not be significant difference between Financial Rate of Return and Economic Rate of Return, as, while formulating the project, factors like price controls, subsidies and tax breaks from local government and also socio-economic benefits have not been taken into account.

11.3 Socio-economic impact of the project

As mentioned above, the concept of ERR is not quite relevant for this project and the impact of the proposed unit would not be quite visible in the overall economic scenario of Bhutan. However, over a long time horizon and setting up of a number of similar units would result into following socio-economic benefits for the country.

- Indigenous production of pharmaceuticals would lead to self-reliance in the field of healthcare services. This would also insulate the medical healthcare services from vagaries of external economies.
- Local production of pharmaceutical would lead to **import substitution** which would result in saving of foreign exchange. Setting up of more units to meet the requirement of hospital supplies would have a multiplier effect on foreign exchange saving.
- There are possibilities of export of the pharmaceuticals to eastern and north-eastern parts of India and other neighboring markets. This would lead to earning to foreign exchange for the country.
- There are not many medium and small scale units manufacturing units in Bhutan. Setting up of a pharmaceutical unit would have a catalytic effect on growth of entrepreneurship in medium and small scale sector.

- The setting up of the project would lead to generation of direct and indirect employment, both for skilled and unskilled workers which would result into economic upliftment of local population. This would also lead to upgradation of skills.
- There are employment opportunities in the project for persons with managerial, technical, financial and marketing capabilities. The employment of such people in the local industry would provide them an option to have an employment in private sector in Bhutan and also reduce the migration of qualified manpower.
- There would be revenue generation for the local government by way of excise, sales tax/VAT and income tax from the unit as well as from its promoters.
- Finally, the project would lead to enhancement of economic activities in the field of construction, transport of raw materials and finished goods, marketing and trade, repairs and maintenance, etc.

It is important here to mention that above benefits can only be listed but these cannot be quantified based on a single unit with small investment. However, as mentioned above, if a number of such units in healthcare sector or any other sector of economy are setup, these would have a significant impact on overall economy of Bhutan.

Annexures

Annexure I

List of machines and equipments suppliers

1. **M/s Cadmach Machinery Co. Ltd.**
7 K, Gopala Tower, 7th Floor, 25,
Rajendra Place, New Delhi 110 008, India
Telephone: + (91)-(11)-5742842

2. **M/s Harrison's Pharma Machinery Pvt. Ltd.,**
4648/21, Shedumal Building,
Darya Ganj, New Delhi – 110002
Tel: 23278924, 23275631

3. **M/s Hindustan Pharmaceutical Equipments Co.**
49, B. T. Road, Narendra Nagar,
Calcutta 700 056, India
Telephone: + (91)-(33)-5532701
Fax: + (91)-(33)-5531436

4. **M/s Grovers International**
3, F4 Shankardham, Sundervan Complex,
Andheri W, Mumbai 400 053, India
Telephone: + (91)-(22)-6313092
Fax: + (91)-(22)-6313014

5. **M/s Genesis Automation Pvt. Ltd.**
11 A-B Soundarajan Street
T. Nagar, Chennai 600 017, India
Telephone: + (91)-(44)-4361023-4321866
Fax: + (91)-(44)-4321866

6. **M/s Gaylord Engineers**
Andheri (E), Mumbai 400 069, India
Telephone: + (91)-(22)-8367168
Fax: + (91)-(22)-8216032

7. **M/s Europack Machines (India) Pvt. Ltd.**
Akash Business Centre, Cst Road, Kurla (W),
Mumbai 400 070, India
Telephone : +(91)-(22)-8502151-8526477

Fax : +(91)-(22)-6505368

8. **M/s Dry Conn Engineering (P) Ltd.**
W 376, II Avenue, Anna Nagar West Ext.
Chennai 600 101, India
Telephone: + (91)-(44)-6262967-6232595
Fax: + (91)-(44)-6262967

9. **M/s Chuliwal Container Pvt. Ltd.**
608-B, I.T.L, twin tower, Netaji Subhash palace,
North Ex Pitampura, New Delhi 110 034, India
Telephone: + (91)-(11)-5489484-5489475

10. **M/s Chitra Engineers**
23, Narmada Estate, N.H. No. 08, Odhav,
Ahmedabad 382 415, India
Telephone: +(91)-(79)-2891666

11. **M/s Jai Agencies**
A-7, Bima Nagar Chs Nagar Chs Ltd.,
Off Sir M.V.Road Andheri (East),
Mumbai 400 069, India
Telephone: + (91)-(22)-8217974

12. **M/s Bhatt Enterprises**
22-781, Subhash Nagar, Chembur,
Mumbai 400 071, India
Fax: +(91)-(22)-5583925

13. **M/s Arctic Sales Asia**
20, Rajpur Road , Civil Lines,
New Delhi 110 054, India
Telephone : +(91)-(11)-2912800

Annexure II

List of raw materials suppliers

1. **M/s Lupin Laboratories Ltd**
159, CST Road, Kalina, Santacruz (E)
Mumbai-400098, Maharashtra
Phone: 022-6525730

2. **M/s Gujarat Lyka Organics Ltd.**
Acme Plaza, Opp. Sangam Cinema
Andheri-Kurla Road, Andheri (E)
Mumbai-400059, Maharashtra
Phone: 022-28238713

3. **M/s Zydus Cadila Healthcare Ltd.**
Zydus Tower, 5th Floor
Satellite Cross Road
Ahmedabad-380015, Gujarat
Phone: 079-26770100

4. **M/s Alembic Limited**
Alembic Road,
Vadodara-390003, Gujarat.
Phone: 0265-2280550

`5. **M/s Hindustan Antibiotics Ltd.**
Pimpri, Pune-411018,
Maharashtra.
Phone: 020-27476522

6. **M/s Torrent Gujarat Biotech Ltd.**
“Torrent House”, Off: Ashram Road,
Ahmedabad-380009.
Phone: 079-26585090, 26580371,

7. **M/s Dr. Reddy’s Laboratories Ltd.**
7-1-27, Ameerpet,
Hyderabad-500016, Andhra Pradesh.
Phone: 040-23731946

8. **M/s Sarabhai M Chemicals**
(Division of Ambalal Sarabhai Enterprises Ltd.),
Gorwa Road, P.B. No. 3580,
Vadodara-390007 (Gujarat).
Phones: 2382433

9. **M/s Parag Pharmaceuticals India P. Ltd.**
203/204, T.V. Ind. Estate,
S.K. Ahire Marg, Worli,
Mumbai-400025, Maharashtra.
Phone: 022-24924710

10. **M/s Uni-Chem Drugs**
No. 7, South Gangai Amman Koil
1st Street, Choolaimedu,
Chennai-600 094
Phone: 044-24801005, 23722835
Fax: 23722835

11. **M/s Cilpa Limited**
289, Belasis Road
Mumbai Central
Mumbai-400008, Maharashtra
Phone: 022-23095521, 23082891

12. **M/s Max India Ltd.**
Plot No. 18, 56, 57, 58,
Kiabd Industrial Area
Nanjangud, Mysore-571301, Karnataka
Phone: 08221-24934564, 24937845,

13. **M/s Alpha Remedies Pvt. Ltd.,**
65, Dharampeth Extension,
Shivaji Nagar, Nagpur-440010

14. **M/s Dinesh Pharmaceuticals Pvt. Ltd.,**
Yamunakunj, Mahavir Colony,
Rajmahal Road, Baroda-390001

15. **M/s Jehovah Organics**
Kakarolia-389390,
Tal. Jambughoda, Distt- Panchmahals, Gujarat

Annexure III

List of lab testing equipment suppliers

1. M/s Imperial Lab Equipment
   Address: 109, Vardhman Plaza Tower, H-3, Netaji Subhash Place
   District Center, PitamPura, New Delhi, Delhi
   Phone(s): 91-11-65154406 / 42470203
   Fax(s): 91-11-27352924

2. M/s Scientific Engineering Corp
   Address: 3280, Arya Pura Old Subzi Mandi, Delhi – 110007
   Phone(s): 91-011-23829918 / 23823794
   Mobile: 9811569035
   Fax(s): 91-011-23829918 / 23823794

3. M/s Toshniwal Brother Pvt. Ltd.
   388 Udyog Vihar Phase 3
   Gurgaon – 122006
   Haryana
   Ph +91-124-4003629 / 4003985
   Fax no +91-124-4003986