3 Plant Profile

1. *Nigella sativa* Linn

General description of plant	
Vernacular names	
Hindi, Urdu	Kalaunji, Kalonji
English	Black cumin, Black seed
Sanskrit	Upakunchika
Gujarati	Kala dungadi beej
Marathi	Kale jeere
Bengali	Kalo jira
Tamil	Karuppu yel
Telugu	Nalla vittanalu
Malayalam	Karanjirakam
Taxonomical Classification	
Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Ranunculales
Family	Ranunculaceae
Genus	*Nigel*
Species	*N. sativa*

Fig. 3-1 *Nigella sativa* Linn. Flower and capsule

3.1 Morphological description of *Nigella sativa* seed[(75)]

It consists of dried seed of *Nigella sativa* Linn. belonging to family Ranunculaceae

Nigella sativa plant is an annual flowering plant grows up to 20-90 cm length. Plant has finely divided leaf arrangement. Flower of Nigella plant has various colors; White, yellow, pink, pale blue or pale purple depending upon the region where it grows. Indian *Nigella sativa* plant has prominently white and pale purple color, with 5-10 petals.

Dried seeds of *Nigella sativa* were selected in the present study for preparing aqueous extract of seeds as one of the treatment options for **RA and associated cardiovascular complications in rats**. *Nigella sativa* seeds have a special large and capsule like sack inflated which has 3-7 united follicles, each follicle contains several seed. This capsule is utilized as it is for culinary purposes and when capsule is fully matured and dried, seeds were collected.

General appearance of whole seed-
Color- Black
Odor- Slightly aromatic
Taste- Bitter
Macroscopic characteristics
Seed shows small, dicotyledonous, trigonus, angular, tubercular, and having externally black and internally white color appearance.
Powder- Powder of nigella appears black, oily to touch generally and under microscope it shows group of parenchyma, endosperm cells and oil globules.
Microscopic characteristics
Seeds shape in microscopic vision have oblong, angular, rugulose tubercular structure which has a small funnel shape with diameter of 0.2 cm. in length and 0.1 cm. in width.
When we cut transverse section of seed it shows single layer of epidermis which consisting of elliptical, thick-walled cells and they are covered externally by a papillose cuticle, filled with reddish-brown pigmented content.
Below pigmented layer, parenchyma composed of thick-walled rectangular, radially elongated cells, present in a layer.
Epidermis of seed is clearly visible and it followed by two to four layers of thick-walled, tangentially elongated, parenchymatous cells.
Endosperm consists of moderately thick-walled, rectangular to polygonal cells, a few filled with oil globules, embryo embedded in endosperm.

Fig. 3-2 Seeds of *Nigella sativa* powder and extract

3.1.1 *Nigella sativa* Plant Cultivation

3.1.2 *Nigella sativa* is an annually growing plant which is 20-90 cm tall at full maturity. It is native to Southern Europe, North Africa and Southwest Asia. Plant also found in Middle Eastern Mediterranean area, South Europe, India (Punjab, Himachal Pradesh, Bihar and Assam), Pakistan, Syria, Turkey and Saudi Arabia.

3.1.3 Conditions for cultivation of *Nigella sativa*

Western Asia and India is major cultivator of *Nigella sativa* plant which required warm environmental conditions for growth along with, adequate sunlight and depleted soil. Light (sandy), medium (loamy) and substantial (mud), all kinds of soil are suitable for plantation and growth. The pH conditions are also equally important for proper growth of plant. The best suited Indian and western Asian countries discovered the culinary use of nigella seeds as a spice, confectionary and for baking industries.

Seeds are the major part of interest for aromatic oil extraction which is widely used in medicinal and cosmetic preparations. Flowering of plant occurs in July and seed collection is done in September.

3.1.4 Chemical constituents of *Nigella sativa* seed[27, 76]

The major constituent of medicinal interest present in Nigella seed is Thymoquinone which is nearly 30%-48% of other phytochemical.

Isoquinoline alkaloids (Nigellicimine and Nigellicimine N- oxide) and indazole ring bearing alkaloids (Nigellidine and Nigellicine) are other constituents of the seed.

Thymohydroquinone, dithymoquinone, p-cymene, carvacrol 4-terpineol tanethol, sesquiterpene longifolene, α-pinene and thymol and some water soluble pentacyclic triterpene and saponin, alpha-hederin also present in the seed.

Oil of seed is highly used components and it is rich in nutritional properties. Aromatic oil of *Nigella sativa* seed is rich in micro nutrients, macro nutrients, protein as well as saturated and unsaturated fatty acids essential for normal health.

3.1.5 Medicinal and Pharmacological properties of *Nigella sativa* seed[29, 75]

Nigella sativa seeds shows numerous pharmacological activities which are evaluated by diverse researchers. Nigella seeds are reported as an ancient remedy in Ayurveda and Unani

medicinal practices. The holy Bible and the holy Quran has accounts of uses of these ***seeds of blessing***. The seed has study accounts for treatment of common wound to the cancer cell inhibiting properties which make this ordinary spice a potent medicinal herb and known as a wonder drug in Ayurveda and Unani medicinal system. Following are the some of the important activities of *Nigella sativa* revealed in different era of time.

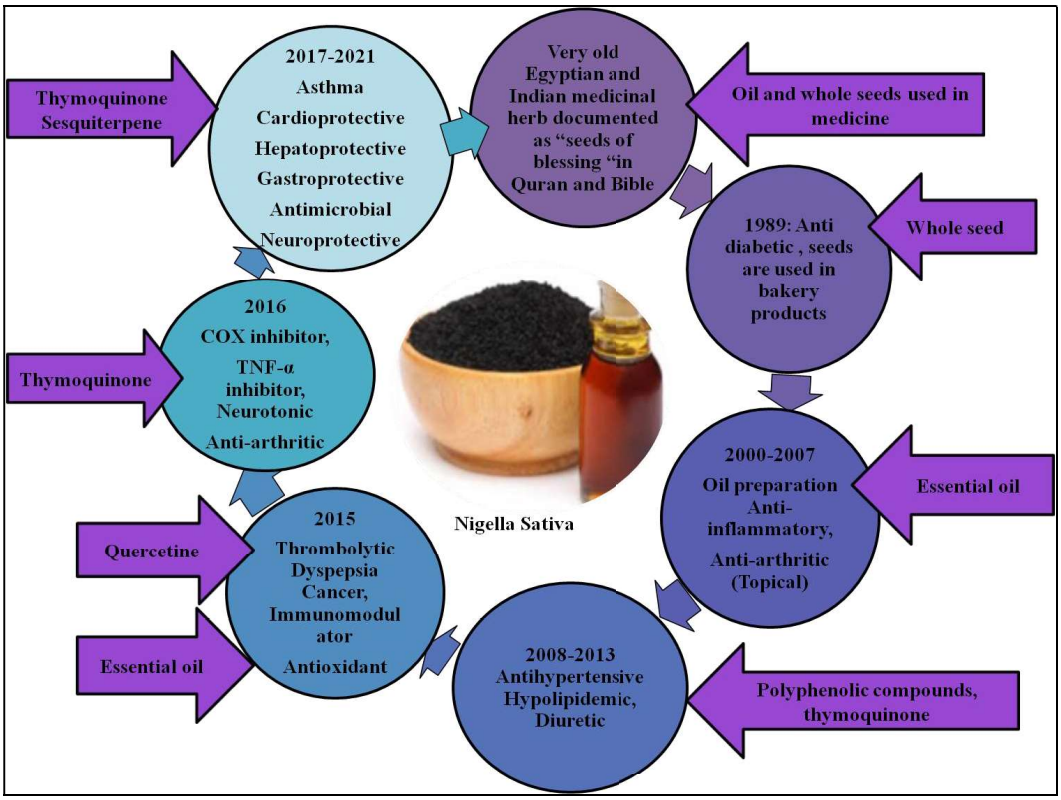

Fig. 3-3 Important pharmacological activities of *Nigella sativa*

3.1.6 Brief description of pharmacological studies of phytoconstituents of *Nigella sativa* seed [28, 77, 78]

3.1.6.1 Anti bacterial activity

Different extracts of *Nigella sativa* seed (aqueous, methanolic, chloroform and diethyl ether extract) shows activity against different gram negative as well as gram positive microorganisms which includes; *S.aureus, E.coli, Pseudomonas aeruginosa, Klebseilla pneumoniae* and *Proteus vulgaris*. Ethanolic extract of seed is proven antibacterial activity

against Methicillin Resistant *S.aureus* (MRSA). All the strains of MRSA were sensitive to extract in concentration of 4 mg/disc as per the research conducted on different micro organisms.

3.1.6.2 Gastro-protective activity

Nigella sativa seed oil and Thymoquinone proved to show anti ulcer properties against ethanol induced gastric mucosa lesions on male wistar rats. Thymoquinone also found effective against absolute alcohol mucosal damages and promote ulcer healing as it reduces the formation of Thiobarbituric Acid Reactive Substances (TBARS). It also increases lipid peroxidation, GSH, SOD and GST which also proves its anti-oxidant potential.

3.1.6.3 Hepatoprotective activity

Hepatoprotective effects of *Nigella sativa* seeds were proved against different study models of hepatotoxicity which comprises D-Galactosamine, LPS, CCL4, INH and Malathion (Insecticide) induced hepatic damages. Alcoholic extract also shows the significant increase in Serum Aspartate Aminotransferase (AST), Alanine Transaminase (ALT), and Alkaline Phosphatase (ALP). Lipid peroxidation and decrease in albumin, albumin/globulin ratio, total protein and NSO or vitamin E administration showed role in the improvement of liver function tests, lipid peroxidation, and antioxidant enzymes.

3.1.6.4 Cardiovascular activity

Nigella sativa seed oil is studied for the cardio-protective effects of the herb which shows activity against cyclosporine and isoproterenol induced cardiac injury and myocardial infarction. Thymoquinone is also proved significantly effective in isoproterenol induced cardiac injury and it was found to reduce plasma SOD and myocardial GSH/GSSG ratio in some cases it also decreases the COX-2 expression in heart cells. Histolopathological changes were also proved to reduce the changes in treatment group.

3.1.6.5 Antidiabetic activity

Nigella sativa is also proven to be a hypolipidemic agent and it also proven for sudden weight reduction. The preclinical as well as clinical research shows the anti-diabetic potential of these wonder seeds. Preclinical studies performed on streptozotocin induced rat model of Diabetes showed a remarkable effect of oral administration of seed on Fasting Blood glucose level of rats. In another study when Aqueous extract of *Nigella sativa* 2gm/day (6 weeks) is compared with Metformin 300mg/kg is also proved to improved glucose tolerance test in rats.

In this study evaluation was done on the basis of metabolic markers including TG, TC, Cholesterol, LDL, ALT, AST and uric acid.

Clinical trials also proved the anti-diabetic effects of *Nigella sativa* seed by reducing the insulin resistance and these seeds showed the increased β cell functions when patients were given powdered seeds in 2gm/day dose.

3.1.6.6 Immounomodulatory effect

Whole seed extract of *Nigella sativa* is established as an Immounomodulatory drug due to evaluation in various trials. Extract and its protein components have potency to inhibit different cytokine release which is majorly involved in the various pathways of immunological as well as auto immune disorders. Seed extract shows activity against B-cells, T-cells and cytokines. Oil of *Nigella sativa* seed also protects the generation of leukocytes and membrane lipid peroxidation. This miraculous spice and Neutraceuticals is also tried for management of COVID-19 pandemic.

3.1.6.7 Anti Cancer activity

Anti tumor activity of *Nigella sativa* was demonstrated in breast cancer cell lines (MCF-7, MDA-MB-231 and BT-474) and some in-vivo studies as well as the human carcinoma cell lines from different tissues; Lung, Liver, Colon, Melanoma and Breast cancer on mice were also performed in which Thymoquinone and different extracts on Nigella seed were potentiated cytotoxic effects of chemotherapeutic regimen (Doxorubicin and 5-Fluorouracil).

3.1.6.8 Anti-inflammatory effect

Nigella sativa seed as well as stems get a place in the alternate anti inflammatory agent as compare to synthetic molecules. Seed extract is active against Carrageenan-induced paw edema and mice model of inflammation which includes acetic acid-induced writhing, formalin and light tail flick tests. The anti inflammatory effects of *Nigella sativa* were due to antioxidant and nitric oxide release inhibitory properties. Thymoquinone also shows effects on inhibitory effect on cyclooxygenase-1 (COX-1) expression, prostaglandin E2 (PGE2) production.

3.1.7 Toxicity account of *Nigella sativa*[(79)]

Nigella sativa is commonly used spice and its oil is being used from ancient time as an anti-inflammatory agent, wound healer and hair growth promoter. The folklore and traditional remedies often have a strong historical evident by passing the culture inheritance but in present scenario scientific accounts for components used as medicinal agent is equally

important to impart the gap between wisdom of ancient era and knowledge of present advancements.

Different toxicity profile of nigella seeds were performed and these seeds were proven safe in these studies up to 800mg/kg doses in animals and 4 gm to 20 gm doses in human were found safe for consumption.

In this present study *in-vivo* toxicity was not performed to prove the safety accounts of the selected herb as nigella seeds have already strong evidences of toxicity accounts in rodents and other species as well as clinical trials also performed on the select Neutraceuticals. The doses of the drug were selected as 100, 200 and 400mg/kg which are very low then the suggested higher doses (1000mg/kg) in rodents.

The following Table 3-1 gives the account of toxicity studies performed on nigella seeds.

Table 3-1 Toxicity account of *Nigella sativa* oil, extracts and crude seed

Sr. no.	Substance	Study	Route	Dose	Outcome	Remark
1.	***In-vivo* study in Swiss albino mice**		i.p.	0.25mg/kg 0.5 mg/kg 01 mg/kg 02 mg/kg 03 mg/kg 04 mg/kg	LD_{50} value	Observation was done for 24 hrs where volatile oil proved to have some behavioral changes in the animals and aqueous extract and fixed oil found safe and no mortality was found
	Volatile oil,	1. Acute toxicity			1,853 mg/kg	
	Aqueous extract				3,020 mg/kg	
	Fixed oil				3,371 mg/kg	
	Aqueous extracts	2. sub acute toxicity	Oral (p.o.)	10ml/kg	Increased ALT levels, unchanged ALP and normal histopathology of liver	Male SD rats were given this dose for 30 days
			Oral (p.o.)	6g/kg/day	No toxicity wide margin of safety	14 days to male and female mice and no toxicity was observed
	Crude Powder of *Nigella Sativa*	3. sub chronic toxicity	p.o	20 g/kg 100g/kg	No toxicity was observed	Powdered drug was added in diet of 7 day old chicks for 7 weeks and no toxicity was observed

2. Carica Papaya Linn

General description of plant	
Vernacular names	
Hindi	Papaya, Papita

English	Papaya, Pawpaw
Sanskrit	Erandkarkati, Madhukarkati
Gujarati	Papaya
Marathi	Papai
Bengali	Papaya, Pepe, Papita
Tamil	Pappali kai
Telugu	Boppayi Pandu
Malayalam	Kappanga
Taxonomical Classification	
Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Brassicales
Family	Caricaceae
Genus	*Carica*
Species	*Carica Papaya* L.

Fig. 3-4 *Carica papaya* Linn. Seed and plant

3.2 Morphological description of *Carica papaya* seed[30]

It consists of mature dried seed of *Carica papaya* Linn. Belonging to family Caricaceae

Papaya plant is herbaceous perennial single stemmed tree having 20–30 feet height. The lower trunk contains conspicuous scars of leaves and fruits. The leaves are large (50 - 70 cm in length and 20 - 28 inch in diameter) and deeply palmately having seven lobes entire margins and petioles of 1-3 feet in length. Papaya plants are dioecious or hermaphroditic, which can produce only male, female or bisexual (hermaphroditic) flowers. Flowers are solitary or small cymes of 3 individuals. Papaya fruits are axillary on the main stem, they grow as a single fruit but sometimes they have small clusters. These are big oval in shape and have a central seed cavity**.** Appearance of fruits is green initially and gradually they turn yellow, red or orange when fully mature in 5-9 months which is totally dependents on temperature and cultivation conditions.

Dried and mature seeds without seed membrane were used in this study to prepare aqueous extract for treatment of RA and its cardiovascular complications in rats.

General appearance of seeds-

The fruit is having a central seed cavity in which large number of seeds presents. The seed coat has a mucilaginous thin membrane sack which is filled with fluid.

- **Color** - Black
- **Odor**- Slightly aromatic
- **Taste**- Sharp , Spicy, bitter and bit salty

Macroscopic characteristics

The fully ripped papaya seeds are clave shaped black seeds with wavy hilum and margins. The size of seeds is 0.6cm in length and 0.4 cm in width.

Powder- Powder of seed is fine with brown to dark black in color with characteristic odor.

Under microscope this powder shows the oil globules, sclerenchyma cells, misocarp endosperm and crystals of calcium oxalate.

Microscopic characteristics

Transverse section of seed is when examined under microscope it shows the single layer epicarp, misocarp, testa and endocarp. The oil globules, calcium oxalate crystals and sclerenchyma are present in inner most endocarp cells.

Fig. 3-5 Seeds of *Carica papaya* powder and extract

3.2.1 *Carica papaya* Plant Cultivation

Carica papaya is tropical plant and it is believed to be originated from southern Mexico and Central America. At present, numerous cultivators are available for the different varieties of papaya plant. India is one of the major producers of the papaya fruit. Apart from India, Hawaii, Tropical Africa, Philippines, Ceylon, Malaysia and Australia also are pioneer in cultivating the papaya tree.

3.2.2 Conditions for cultivation of *Carica papaya*

Carica papaya plant is fast growing plant and simple seed propagation method is used for cultivation. It needs Tropical, Sub-Tropical and Monsoonal climate for proper growth. Sandy and well drained soil is preferable for suitable cultivation of the plant. Thee Suitable cultivation period for plant in India is February - March, June-July and October-November.

3.2.3 Chemical constituents of *Carica papaya* Seed

- *Carica papaya* seed is rich in **fatty acids, crude proteins** and **crude fibre.**
- *Carica papaya* **seed oil** is one of the major constituents of seed which is responsible for the medicinal properties of seed.
- *Carica papaya* seed contains major phenolics such as ***p*- Coumaric acid, Kaempferol-3 glucoside, p-Hydroxybenzoic acid, Quercetin-3-galactoside, caffeic acid** and **ferulic acid.**
- Phytosterols such as **Campesterol, Stigmasterol** and ***β*- sitosterol** are major chemical components accounted to give medicinal activity.
- *Carica papaya* seeds also have enzyme **Nyrosin** which is different from Papain obtained from fruit.
- **Benzylisothiocynate** also present in *Carica papaya* seed which is a sulfur rich compound.

- **Carpaine, benzylglucosinolate** and **glucotropacolin, benzylthiourea, hentriacontane** and **caricin** are also present in seeds.
- **Flavonoids, sterols, terpenoids, glycoside, anthraquinones** and **phlobotannins** are other phytochemical present in *Carica papaya* seed.

3.2.4 Medicinal and Pharmacological activities of *Carica papaya* seed[80]

Carica papaya plant is widely used as a raw and ripe fruit in almost all corners of the world. Fruit, leaves and seeds are the majorly used parts of the plant for different purposes. Distinguish enzymes obtained by the plant are having significant place in the chemical and pharmaceutical industry. Plant is having a special recognition in Ayurveda, Naturopathy, and Neutraceuticals and in Cosmetics due to healing and rejuvenating properties. The plant is equally contributes is pharmacology with its medicinal uses, among which some of them are listed here in brief and the histological account of uses of seed is depicted in the following figure-

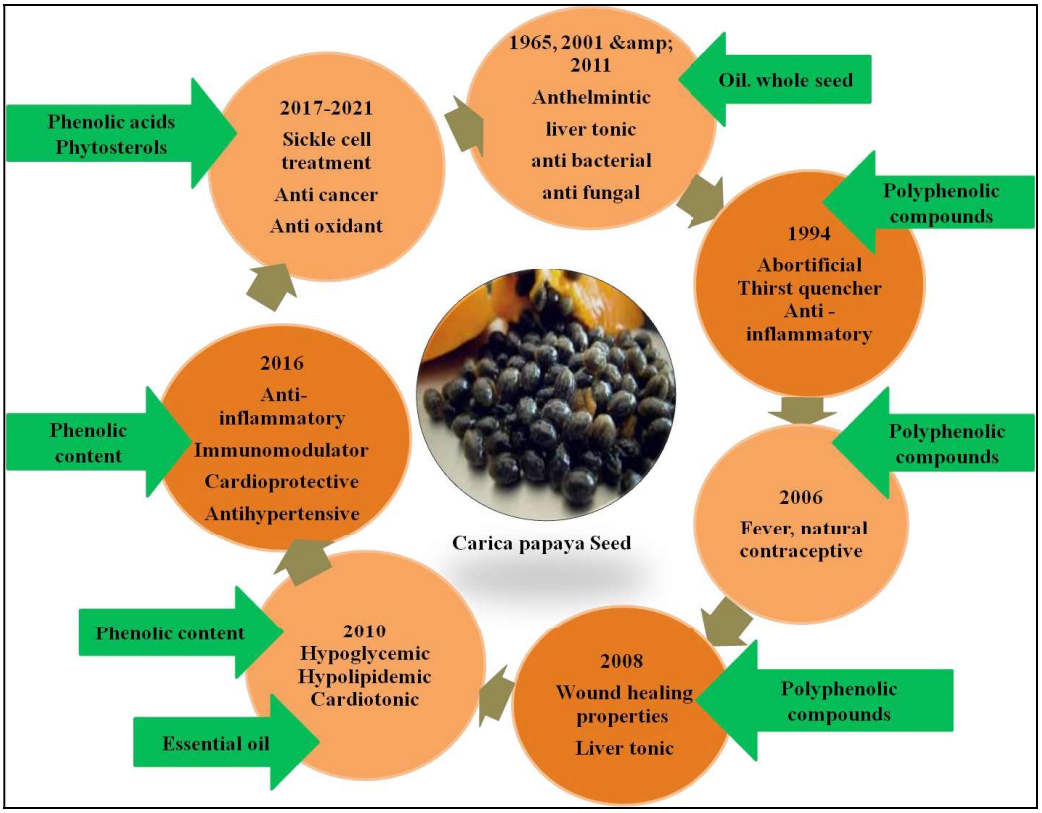

Fig. 3-6 Important pharmacological activities of *Carica papaya*

3.2.5 Brief description of pharmacological studies of phytoconstituents of *Carica papaya* seed-

3.2.5.1 Anti Diabetic activity

Carica papaya seeds have account for traditional usage in treatment of Diabetes. To evaluate this activity *in-vivo* study was performed on hyperglycemia induced rat where different doses of aqueous and ethanolic extracts of papaya seeds were evaluated against 0.1 mg/kg/day of glibenclamide for 30days. The study showed that, and 100 - 400 mg/kg/day of ethanolic extract of *Carica papaya* seed are effective in lowering the lipid profiles as well as glucose levels.

3.2.5.2 Anti fertility effect in males

Oral administration of *Carica papaya* seeds is one of the ancient methods for natural contraception. Scientifically these seeds produces changes in epididymal epithelium which in turn affects the protein secretion and influences the sperm maturation hence confirmed its reversible contraceptive efficacy.

3.2.5.3 Antioxidant activity

Carica papaya seed possesses a strongest antioxidant activity due to presence of phenolics and total flavanoids components. Crude seed powder and different factions of *Carica papaya* seed extracts (aqueous, ethanolic, methanolic and chloroform) are reported to show antioxidant properties in different studies denoted by lowered lipid peroxidation, enhanced glutathione levels, and reduction of activity of catalase and superoxide.

3.2.5.4 Anti inflammatory activity

Carica papaya seed oil is responsible for tissue repair which is used as an anti aging agent. The saponin present in seed is responsible for the anti inflammatory activity. Among different fractions of seed extraction, aqueous extract of papaya seed showed higher activity against inflammation on Carrageenan induced paw edema in rats in one of the *in-vivo* studies.

3.2.5.5 Anti Microbial activity

The whole plant of *Carica papaya* having medicinal values and the different parts of plant possess their unique activity. In the literature survey different extract of leaves, roots and seeds of *Carica papaya* showed anti microbial activity against various microorganisms. Seeds of *Carica papaya* in methanolic, benzene, acetone and aqueous extract have showed zone of inhibition against *Staphylococcus aureus, Bacillus subtilis, Escherichia coli* and *Pseudomonas aeruginosa.* Antimicrobial activity of extracts increases as the concentration

increases against all the bacteria. Most of the plant parts show the antimicrobial activity against *Staphylococcus aureus*.

3.2.6 Toxicity account of Carica Papaya[81]

Acute oral toxicity testing

Adeneye *et al*. (2006) reported the acute oral toxicity study as per the OECD Guidelines on Acute Oral Toxicity Testing method (AOT425 Stat Pgm). Study was conducted on wistar male rats weighing 120-150 gm at a limit oral dose of 2000 mg/kg of the extract. No mortality was shown in any of the groups. Weight reduction was observed in some animals.

Nazneen Zehra and Lubna Naz (2020) revealed the safety profile of *Carica papaya* aqueous seed in different doses. In his study wistar rats were administered with 100, 200 and 400 mg/kg aqueous extract of carica papaya seed for 42 days and the liver function tests were performed against control group where there was no mortality or toxic evidences were observed and the animals showed no other adverse effects. The only change in the animals was the decrease in body weight in the higher dose of CPAE.

3. *Momordica charantia*

Vernacular names	
Hindi	Karela, Kathilla
English	Bitter gourd
Sanskrit	Kaarvellakah
Gujarati	Karelu
Marathi	Ambalem
Bengali	Karala
Tamil	Iracavalli
Telugu	Kakara
Malayalam	Kayppa, Pavaykka
Taxonomical Classification	
Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Cucurbitales
Family	Cucurbitaceae
Genus	*Momordica*
Species	*M. charantia*

Fig. 3-7 *Momordica charantia* seed and plant

3.3 Morphological description of *Momordica charantia* seed[82]

It consists of dried mature seed of *Momordica charantia* family Cucurbitaceae

Momordica charantia plant is an annual creeper. It is herbaceous, slender climber with slightly pubescent stems and leaves of the plant are 1-3 inch wide is parted in 5-7 parts. Flowers of momordica are yellow and monoceous. *Momordica charantia* plant has obovoid or oblong-cylindrical shape fruits. Outer surface of fruit is coarsely ridged and have bumpy-tuberculation. Mature fruit can be 2-10 inch long having green color and barrel shape with thick middle part and sharp at the edges.

In the present study ***Momordica charantia*** **seeds without seed coat were used as a crude drug and the aqueous extract of these seed was used for management of RA and its cardiovascular complications.**

Momordica charantia seeds are covered with a soft, fleshy red aril and they are 12-16 mm long and appear white in unripe fruits, Seed coat appears red on ripening and after drying the turned to brick red and after removing the seed coat white colored flesh is obtained.

General appearance of whole seed-

- **Color-** Off white, slight brown
- **Odor-** Characteristic
- **Taste-** Slightly bitter

Macroscopic characteristics

Appearance of *Momordica charantia* seed is oblong and grooved surface with a sculptured surface. Seed contains a tough seed coat with multiple layers.

Microscopic characteristics

The transverse section of seed under microscope appears to contain structured epidermis, hypodermis, sclerenchyma, arenchyma and chlorenchyma. Epidermis consists of leaf shaped cotyledons which are present on the inner surface of epidermis and they are separated in two parts with a palisade layer, this part of the seed contains the oil globules and protein granules.

Fig. 3-8 **Seeds of *Momordica charantia* powder and Extract**

3.3.1 Conditions for cultivation of *Momordica charantia*

Bitter melon plant originated from south Indian state Kerala. Now a day's plant is cultivated throughout India as a vegetable crop. It also found in China as it was introduced there in 14th century. It is widely used in the cuisines of East Asia; South Asia and Southeast Asia.

The most suitable cultivation time for bitter melon crop is rainy season and summers. This climate is prominent in northern Indian areas which is preferable for cultivating the fruits nearly throughout the year. The growth, size and shape of fruits is solely depends upon the habitat and the maturation period of plant. The creeper cultivated in summers (March - April) has more strength and they do not need support to grow. On proper watering and manure based soil the fruit is ready for collection within 30-35 days. The rainy season crop (June-July) needs support to grow and to get mature. The fruit is commonly collected for culinary purposes as vegetable and the seed of plant as well as skin of fruit is used in different cosmetic and medicinal purposes.

3.3.2 Chemical constituents of *Momordica charantia* seed[33, 83]

- Plant contains various phytoconstituents like **glycoside, Alkaloids, saponin, fixed oils, sesqueterpenoids** and **triterpenoids.**
- **Cardiac glycoside diosgenin** present mainly in fruit and seeds
- Seeds of *Momordica chirantia* also contain ***p*-Insulin, α and β glycoproteins (Momorcharins), charantin, charine, cryptoxanthin, cucurbitins** and **cucurbitacines.**
- **Cytokinines** and **lectins** also found in seeds which posses different medicinal activities.
- Presence of Amino acids such as; **valine, threonine methionine, isoleucine, leucine, phenylalanine, glutamic acid** also reported in the seeds of *Momordica charantia.*

- **Seed oil** also contains saturated fatty acids mainly **stearic acid, monounsaturated fatty acids** like **linoliec acid** and **poly unsaturated fatty acids.**

3.3.3 Medicinal and Pharmacological properties of *Momordica charantia* seed[83]

Momordica charantia is one of the oldest plant used is natural Indian medicinal system. Leaves, fruit and seeds are the major parts used as therapeutic agent. The Fruit is used as a vegetable in certain parts of the world. As in ancient system of the treatment edible things were used for management of different condition as home remedy, all parts of fruits and vegetables were revealed by the people. Traditional medicine has a reserved place for such ancient treasures where bitter melon is used for the inflammation, wound healing, anti diabetic and as a bitter tonic.

This pictorial representation of *Momordica charantia* seed shows the evolution for its medicinal uses-

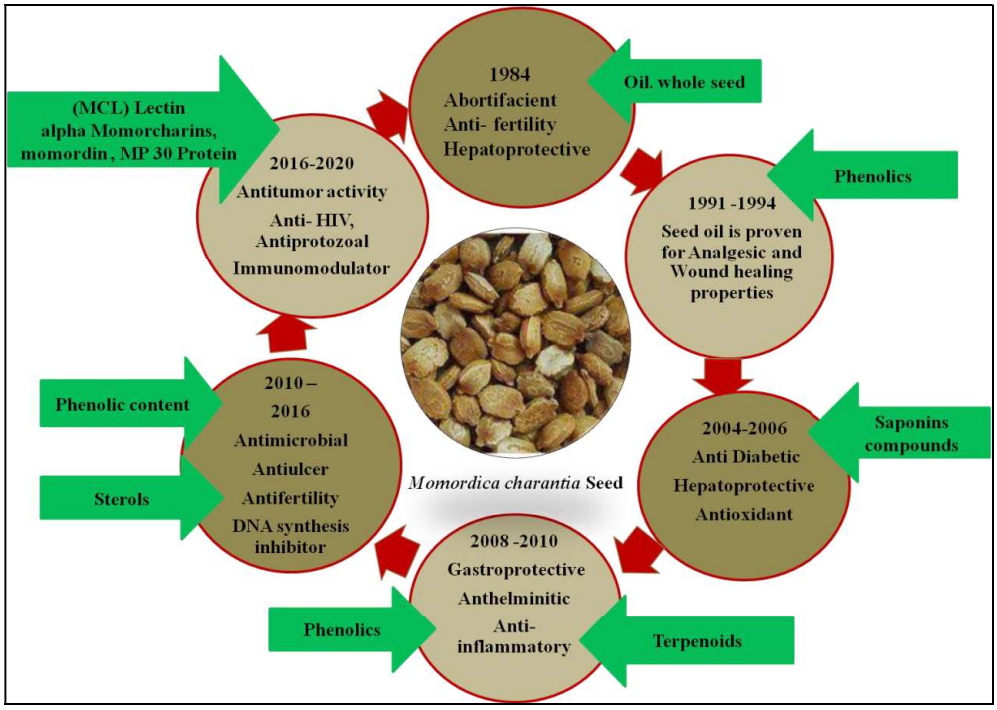

Fig. 3-9 Important pharmacological activities of *Momordica charantia*

3.3.4 Brief description of pharmacological studies of phytoconstituents of *Momordica charantia* seed-

3.3.4.1 Antioxidant activity

Phenols, saponins and polysaccharides are the major components present in the seeds which are reported for possessing antioxidant properties in different *in-vivo* and *in-vitro* experimental conditions. Aqueous and ethanolic extracts were reported as strong antioxidant agent in various *in-vitro* models. In different experimental conditions, the significant increase in SOD, CAT and GST was noticed. In another study conducted by Sathishsekar et al., 2005 seeds were proved in effectively normalize the impaired antioxidant status in streptozotocin induced-diabetes.

3.3.4.2 Antidiabetic Activity

Momordica charantia fruit is very popular as a traditional remedy for diabetes. Fruit and seeds of *Momordica charantia* are reported to contain P-Insulin which increases glucose uptake and glycogen synthesis in the liver, muscles and fat cells responsible for improvement of blood glucose level. *In-vivo* experiments also shown that karela fruit and seeds improves insulin release from pancreatic beta cells, and helps in repairing and promote new growth of insulin-secreting beta cells in rat. This activity is due to presence of phytoconstituents; charantin, vicine, glycosides and karavilosides when these phytochemical act with P- Insulin they reproduce hypoglycemic activities.

Moreover Lectin (known as *Momordica charantia* Lectin or MCL) and Chirantin present in Momordica mimics the insulin like actions on linking with insulin receptor which activates the peripheral uptake of glucose to maintain the blood glucose concentration which contributes in hypoglycemic effect after consumption of fruit or seed.

3.3.4.3 Anti inflammatory, Gastroprotective and Immunomodulator

Inflammation and immunological intervention is one of the major factors to cause simple infection to the autoimmune diseases. *Momordica charantia* is one of the medicinal plants which are used from the ancient time in folklore and in traditional medicines for the treatment of wound healing, inflammations and ulcer healing.

According to the newer scientific data the properties of the karela plant and the uses of the different parts of the plant and their extracts revealed the anti inflammatory and immunomodulatory effects of Momordica in experimental prospect.

Xu et. al performed the study on C57BL/6 mice to see the effects of plant and the different extracts on the HFD fed fatty liver conditions. The study revealed the hypoglycemic and

hypolipidemic actions of the plant with the inhibitory effects on IL-6, CRP, IR and obesity. Study also showed that the macrophage infiltration is decreased which is a major initiative for the immune responses. Plant also showed the limiting effects on monocytes chemotactic protein -1 (MCP-1), TNF-α, cytokines (IL-2, IL-6), Matrix Metalloproteinase (MMP-9) levels, NF-κB and protein tyrosine phosphatase expressions in Epididymal Adipose Tissues (EAT). In another experiment Jain and colleagues have investigated the effects of Momordica in the tibial and sural nerve transaction (TST) induced neuropathic pain in rats. Some phytoconstituents present in fruit, leaf and seed also associated with activity against T cell B cell and Th0 helper cell which indicates involvement of plant in immunomodulation.

3.3.4.4 Antineoplastic Activity

Momordica charantia seed have been reported to possess anti neoplastic activities in *in- vitro* as well as *in-vivo* studies.

The seed was proved to give an ameliorative effect on tumor generating factors in cell line studies performed on hepatic carcinoma cells, where different fractions of seed extracts were results in limiting the excessive cell growth via apoptosis, cell cycle arrest, autophagy and inhibition of cancer stem cells.

In studies conducted on mice and rats also the fruit and seed phytoconstituents were found to give cytoprotective and anti neoplastic activities in different cancers (Breast cancer, Lung cancer, hepatic cancer and acute myeloid leukemia).

The triterpenoids present in seeds cucurbitins and other bioactive chemical constituents; triterpene glycosides, phenolic acids, flavanoids, essential oils, saponins, fatty acids, and proteins (MP30) are responsible for these activities.

In other literature search the role of some isolated compounds; Karaviloside, Kuguaglycoside, Momordicoside, Charantin, α-eleostearic acid and proteins like α-Momorcharin and some of the RNase MC2 isolated from the seed are proven effective in Hodgkin's lymphoma, liver cancer, human leukemia, melanoma and solid sarcomas. Karela fruit and other parts of the plant are also demonstrated anti tumor activities clinically due to inhibition of granulate cyclase enzyme which is linking pathway in psoriasis, leukemia and breast cancers.

3.3.5 Toxicity account of *Momordica charantia* seed[(84)]

In traditional uses karela seeds are generally consumed with the fruit as vegetable and no toxic events were observed. Different *in-vitro* and *in-vivo* studies were performed for testing toxicity accounts of fruit as well as distinguish extracts of seed.

Khan et al. proved the toxicity accounts of methanolic extracts of *Momordica charantia* seed on zebra fish embryo on treatment of different dilutions (1 to 400 µg/ml) of extracts for 5 days. Experiment was repeated for three times and concluded that the methanolic fraction of *Momordica charantia* extract is teratogenic in these embryos.

In long term use of seed extract fractions were observed the infertility in different studies performed for anti diabetic effects of seed but teratogenicity or other toxic events were not observed in higher animals.

Seed coat is hypothesized to give toxic events due to lecithin and protein synthesis but the strong evidences are still needed.

In this study the extract was prepared without seed coat and *in-vitro* tests were performed to check the cytotoxic events where the aqueous extract was proved to give cell proliferation.

In traditional usage seed can be consumed in 2 gm doses and in this current study 100, 200 and 400 mg/kg doses of *Momordica charantia* extracts were used which reduced the chances of toxic evidences.

3.4 Plant collection and Authentication

Nigella sativa seed were purchased from a local grocery store from Siyagunj Indore, Madhya Pradesh and *Carica papaya* Seed were collected from Papaya farm Japodad, Gujarat. Dried seeds of *Momordica charantia* were collected from a vegetable field situated at Khargone, Madhya Pradesh. The samples of the crude herbs were identified and authenticated by Dr. Padmanabhi S. Nagar assistant professor department of Botany at The Maharaja Sayajirao University of Baroda, Vadodara. Reference no. for the authentication certificate is **Ref: Bot/30317/aut/1/ TD04** (Annexure III**).**

3.5 Avocation for choosing these particular herbs

***Nigella sativa* Linn (NS)** commonly known as black seeds or Kalonji, well known spice in Indian and Arabian cuisine. NS is placed as an important therapeutic component in almost all traditional or indigenous systems of medicines which includes Ayurveda, Sidhdha, Unani and Tibb systems. Seed of *Nigella sativa* contains Thymoquinone as a major phytoconstituents possessing anti-inflammatory, anti-pyretic, anti atherogenic Anti tumor properties and NS also have potential action against TNF-α, macrophage and neutrophil which generates pro-inflammatory cytokine release.

***Carica papaya* Linn (CP)** seed commonly known as paw-paw seed is categorized as super food. Flavanoids, saponins, tannins, alkaloids, and anthraquinones are its major constituent

which are responsible for its cardio protective, analgesic, anti-inflammatory and wound healing properties.

***Momordica charantia* Linn (MC)** also known as Karela or bitter guard is commonly used vegetable of Cucurbitaceae family and past research suggested the use of fruit having hypoglycemic and hypolipidemic properties. In the present study seed of bitter guard were taken for evaluating their anti inflammatory and anti arthritic activities. Phytochemical constituent present in seeds contains oil, and sterols possesses the anti bacterial anti microbial and anti inflammatory properties.

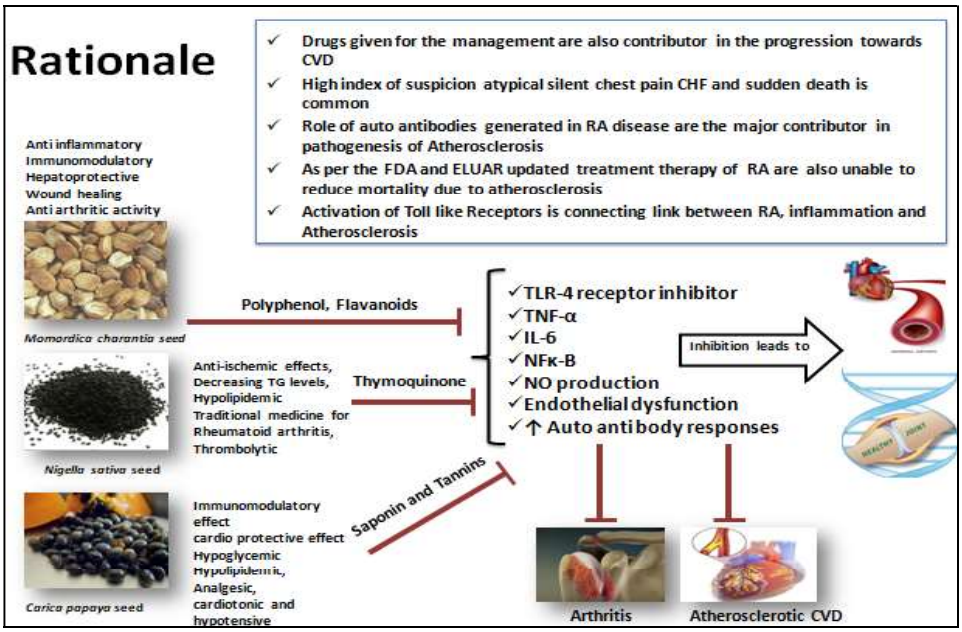

Fig. 3-10 Rationale for select herbs in RA and RA with CVD

All three seeds are chosen for the present study due to their common pharmacological properties which synergistically acts as anti arthritic and Immounomodulatory drugs. As existing therapies for RA have risk associated with cardiovascular complications, this new synergistic combination was hypothesized to relieve cardiovascular complications also along with existing Rheumatoid Arthritis.

Here in this study all the three herbs selected are hypothesized to have anti arthritic and Immounomodulatory effects with prevention of CVD complications initiated with Atherosclerosis and their brief description with compatible effects with each other is showed in following table-

Table 3-2 Brief description of herbs selected

Description	**Herbs**		
	***Nigella sativa* Linn** **(Ranunculaceae)**	***Carica papaya* Linn** **(Caricaceae)**	***Momordica charantia* Linn** **(Cucurbitaceae)**
Part used	Dried matured Seed	Dried matured seed	Dried matured seed
Traditional use	Traditionally used for Rheumatoid arthritis as local application in oil form, Thrombolytic, Anticancer	In folk medicine seeds are used as laxative, Analgesic, antibacterial, amebicide, Cardiotonic and Hypotensive	Traditionally used for wound healing, anti inflammatory as topical therapy
Pharmacological studies for other uses	Anti-ischemic effects, Decreasing TG levels, Hypolipidemic, Antidiabetic, skincare product	Immunomodulatory effect and cardioprotective effects, Hypo-glycemic and Hypo-lipidemic	Hypoglycemic and hypolipidemic properties, anti inflammatory and anti arthritic activities. Anti bacterial anti microbial and anti inflammatory properties.
Chemical constitutes responsible for medicinal properties	Thymoquinone, Polyphenol and Tocopherol, Dithymoquinone, Thymohydroquinone, and Thymol	saponins, tannins, alkaloids, Flavonoids, anthraquinones, glycosides and reducing sugars	Flavanoids, sterols, tannins, glycosides
Rationale for selection for the current study	TNF-α, macrophage and Neutrophil blocking actions, immunomodulatory actions	Anti-inflammatory, analgesic properties	hypolipidemic, anti inflammatory and anti arthritic activities