REVIEW

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Application of differential scanning calorimetry to study the interpretation on herbal medicinal drugs: a review

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Competing interests

The authors declare no conflicts of interest.

Abbreviations

DSC, differential scanning calorimetry; Cp, capacity.

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Abstract

Background: Differential scanning calorimetry as a method of investigating and monitoring the kinetics of herbal medicinal plants. Some instrumental and experimental aspects are discussed. **Methods:** A brief survey is made of herbal medicinal plants and results of differential scanning calorimetry studies are reviewed and this discussion is presented the effects of the instrumental conditions like heating rate and the sample conditions like sample particle size, sample mass, sample purity, sample stability in the melting region and property of impurities. **Conclusion:** This study suggests that application of differential scanning calorimetry to study the interpretation on herbal medicinal drugs.

Keywords: differential scanning calorimetry; medicinal plants; thermal analysis

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Introduction

Thermal Analysis mainly refers to the analysis of properties of materials that change with the temperature and These properties include in thermal analysis technique such as thermal diffusivity, mass, dimensions, mechanical stiffness, dielectric permittivity, optical properties, etc. In other word, thermal analysis involves various techniques that are used to study the changes in chemical or physical properties of materials when they are subjected to heat, i.e., heated, cooled or kept at specific temperature. Along with this providing some of the basic information about the properties of materials, these techniques are also a prominent engineering tool required for the growth of new useful materials. A wide variety of substances, including composites, thin films, polymers, ceramics, metallic glasses etc., can be studied by the thermal analysis techniques. Different properties are studied by different types of techniques of thermal analysis, which are mentioned in (Table 1) [1].

A general instrumentation for the thermal analysis includes shown in (Figure 1) [1]: 1. Sample holder - where the sample is kept; 2. Sensors - for detecting the required properties of sample with respect to temperature; 3. Closed chamber - where the sample and sensors are kept and the experimental parameters can be controlled according to the requirements for study; 4. Computer - for adjusting the experimental parameters, collecting the datas and performing calculations.

Table 1 Different types of thermal analysis techniques

Techniques	Properties measured
DSC	Heat difference
Dynamic mechanical analysis	Mechanical stiffness and damping
Thermo-optical analysis	Optical properties
Dilatometry	Volume
Dielectric thermal analysis	Dielectric permittivity and loss factor
Evolved gas analysis	Gaseous decomposition products
Differential thermal analysis	Temperature difference
Thermogravimetric analysis	Mass
Thermomechanical analysis	Dimension
Laser flash analysis	Thermal diffusivity and thermal conductivity
Derivatography	A complex method in thermal analysis

DSC, differential scanning calorimetry.

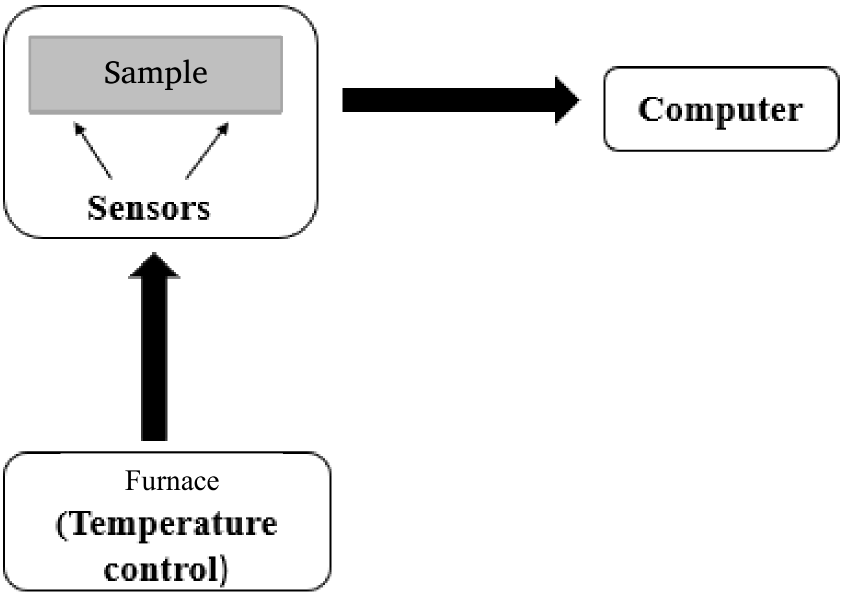

Figure 1 General representation of instrumentation of thermal analysis techniques

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Main text

Differential Scanning Calorimetry (DSC): It is one of the most ordinary thermo analytical technique. E.S. Watson and M.J. O'Neill developed this method in the year of 1962 and commercialized it in the year of 1963 at Pittsburgh Conference on Analytical Chemistry and Applied Spectroscopy [1].

DSC analysis, it is a thermal analysis technique that analyses heat capacity (Cp) of compound by changing the temperature and sample of familiar mass is cooled or heated and the difference of its heat capacity are followed as changes in its heat flow rate. This allows the detection of transitions such as glass transitions, melts, curing and phase changes. Because of this pliability, since almost all materials show some transitions.

DSC method is used in many pilot plants, including food, manufacturing, pharmaceuticals, paper printing, polymers, semiconductors, agricultural and electronic industries. The biggest advantages of DSC are the speed and ease so it can be used to see transitions in almost all materials.

Natural herbal components like seeds, exudates, gums, mucilages, polysaccharides, hemicelluloses, celluloses, and starch etc. are currently known as excipients. Literature study reveals that medicinal, nutraceutical and pharmaceutical use different herbal drugs as in dosage form design. DSC analysis was found to be useful as depiction tool to elucidate and hold up the recovery features of different herbal drugs [2].

In general, three different types of information can be obtained from DSC: 1. The complete partial heat capacity of a substance; 2. General thermodynamic parameters like entropy change [ΔS], enthalpy change [ΔH], and heat capacity change [ΔCp] connected with a temperature induced transition; 3. The divisional function and adjunt the population of intermediate conditions and their thermodynamic parameters [3].

DSC is a thermal analysis apparatus measuring how physical properties of a sample change, along with temperature against time. i.e., the device is a thermal analysis instrument that shows the temperature and heat flow associated with material transitions as a function of temperature and time. Change in temperature, DSC measures a heat quantity, which is radiated or absorbed excessively by the sample on the basis of a temperature difference between the sample and the reference material.

Based on the mechanism of operation, DSCs can be classified into two types: heat-flux DSCs and power-compensated DSCs.

In a heat flux DSC, the sample material is kept in a pan and an empty reference pan are set down on a thermoelectric disk surrounded by a furnace. The furnace is heated at a linear heating rate, and the heat is shifted to the sample and reference pan through the thermoelectric disk. But, owing to the heat capacity (Cp) of the sample, there would be a temperature difference between the sample and reference pans, which is calculated by area thermocouples and the consequent heat flow is determined by the thermal equivalent of Ohm's law;

$$q = \Delta T/R$$

Where, q - heat flow of sample, R - resistance of thermoelectric disk, ΔT - temperature difference between reference and sample.

In a power compensated DSC, the sample and reference pans are put down in different furnaces heated by different heaters. The sample and reference are maintained at the same temperature, and the difference in thermal power required to maintain them at the same temperature is measured and plotted as a function of temperature or time.

DSC is a thermodynamical tool for direct assessment of the heat energy uptake, which occurs in a sample within a regulated increase or decrease in temperature. The calorimetry is particularly applied to monitor the changes of phase transitions. DSC is commonly used for the study of biochemical reactions and which is named as a single molecular transition of a molecule from one conformation to other. Thermal transition temperatures (Tt- melting points) of the samples are also measured in solution, solid, or mixed phases such as suspension.

Experimental condition

In common DSC experiment, energy is found simultaneously into a sample cell which is having a standard with molecule and the reference cell containing only standard. Temperatures of both cells are increased similarly over the time. The difference in the input energy required to match the temperature of the sample to that of the reference would be the amount of excess heat absorbed or released by the molecule in the sample during an exothermic or endothermic process, respectively. As a result of the presence of the molecule of interest, more energy is required to bring the sample to the same temperature as the reference [4].

The schematic representation of DSC is shown in the (Figure 2). The reference and sample pans both are put adjacent to each other and a common heating profile is applied to both of the pans. Both of them are sealed in aluminium pans (or copper) and Reference is commonly an inert material like alumina, or an empty pan with lid. The crucibles used are made up of aluminium, copper, platinum, gold, etc., in order to withstand with the high temperatures applied to them and to avoid any reaction with them. Different atmospheres, such as nitrogen, argon, air, vacuum, etc., can be maintained in order to achieve desired outcome. Both (sample and reference) are connected to a temperature sensor and a heater coil. Heater coil heats them at a constant rate and temperature sensor senses the temperature difference between the sample and reference. Same Linear heating rate is applied to both of them, i.e., temperature is increased at a constant rate. Both the reference and sample are maintained at same temperature.

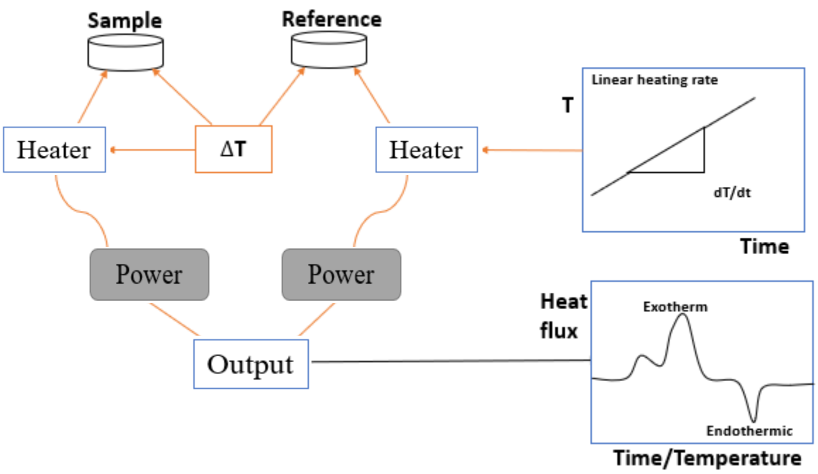

Figure 2 Schematic diagram of DSC. DSC, differential scanning calorimetry.

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When heating is carried out and the sample tends to absorb or release some heat as a result of phase changes occurring in it. In order to maintain the same temperature condition for both sample and reference pans, heat is needed to be supplied to the sample undergoing phase transitions. This amount of heat supplied or taken out determines the exo or endo thermic processes occurring in the sample. The amount of heat transferred to the sample is monitored using a PC and the output is received in form of a thermo-gram showing different exothermic and endothermic peaks. Two different conventions are used to represent the exo and endo thermic processes. Exothermic and endothermic reactions are shown in positive and negative directions respectively, or vice-versa depending upon the kind of conventions used in the instrument.

A classic DSC plot is shown in (Figure 3) [1]. The thermogram can be used to understand many important properties of a material, such as temperature, heat capacity and enthalpy of change in different phases such as glass transition, crystallization, and melting.

Heat capacity: Heat Cp is known to be, the amount of heat required to increase the temperature of a material by 1°C. It can be calculated by the ratio of amount of heat flow and the heating rate. The amount of heat flow is the heat flowing per unit time, i.e

Heat flow = Heat/Time = $\Delta q/t$

Usually heating rate is time rate of change in temperature, i.e,

$$\Delta T/t$$

Where, t and T are time and temperature respectively.

Hence, heat capacity can be written as,

$Cp = q/\Delta T$

Glass Transition: Glass transition is a downward shift in the baseline (Figure 4) [1]. with increase in temperature (or time). This shift in baseline does not occur instantly, rather it takes place over a temperature range. Due to this the determination of the glass transition temperature (Tg) becomes hard and basically it is clear out to be in the middle of the transition. It is an endothermic transition, i.e., it absorbs heat. Hence the heat capacity of the material increases during glass transition.

Crystallization: It is an exothermic event, in which the material releases heat and forms a low energy (stable) ordered structure. The enthalpy of crystallization can be obtained by calculating the area under the peak, and dividing it by the heating rate. Further the percentage crystallinity at a particular degree of conversion can also be calculated. Together with the enthalpy of crystallization and the crystallization temperature, DSC can also be used to determine whether the amorphous material crystallizes in a single step or it takes multiple steps to crystallize.

Melting: As heating of a material is continued beyond crystallization, eventually it melts. Melting is an endothermic process that transforms a solid material into liquid. Crystallization and melting are first order phase transitions since they involve latent heat. Whereas, no latent heat is associated with glass transition, rather it involves an increase in heat capacity. Hence, it is considered to be a second order phase transition.

The advantages of DSC technique can be explained below: 1. Different kinds of sample like liquid, powders, solid, thin films can be tested in a variety of environments (air, vacuum, inert gas, etc.); 2. It is a fast technique, i.e., it takes a small time to perform one run; 3. The applicability of DSC can be extended to a wide variety of materials that includes the pharmaceutical and drug industry, polymers, liquid crystals, and food science. DSC also can be used to determine the oxidative stabilities of the materials; 4. A wide range of temperature is used to analyse the phase transitions in a material, and quantitative analysis of these transitions can be done easily using softwares [1].

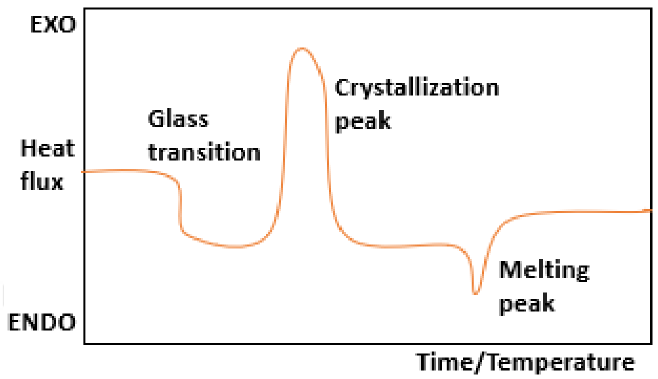

Figure 3 Typical DSC thermogram

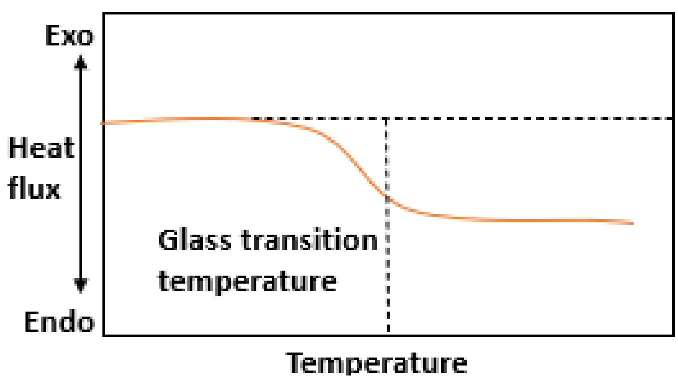

Figure 4 Schematic representation of glass transition

DSC interpretation on herbal drugs

Various research articles, data, and reports published by scientist on DSC interpretation on herbal drugs from medicinal plants were presented in (Table 2).

Conclusions

The movement towards, the analysis of DSC kinetic data by computational methods in the study of herbal medicines plays an important role. Although DSC scans are relatively easy and quick in implementation it is advisable to also obtain isothermal data at several various temperatures. DSC is highly being applied to the study of herbal medicines in combination with other analytical methods such as Fourier transform infra-red spectroscopy, nuclear magnetic resonance and chromatographic analytical methods, and also dynamic mechanical or dielectric studies. It is probably as part of such combinational investigations that DSC can be used most effectively in basic research, and in quality control and assessment study.

Table 2 DSC interpretation on several herbal drugs

Sl. no	Author name	Title of the work	Description of analysis
1	G.S deokar et al.,	Impact of hydrothermal isolation method on the recovery of fenugreek seed hemicellulose analysed through FTIR-DSC-SEM interpretation.	They have reported that hydrothermal isolation method of *Trigonella foenum-graecum* L. hemi-cellulose analyzed by using DSC method by using schimadzu DSC-60 and the study is carried out on isolated hemicellulose component (4.0 mg) powder from heated on aluminium pan with empty reference pan at the rate of 5 °C /min within a 20–300 °C temperature under the condition of nitrogen flow 100 mL/min [2].
2	M. Rajani et al.,	A rapid method for isolation of andrographolide from *Andrographis Paniculata Nees* (Kalmegh)	They have reported a method for the isolation of andrographolide from *Andrographis Paniulata Nees* (Kalmegh) by using DSC by recording the melting point of compound on a DSC to check the purity of isolated andrographolide at the rate of 5° C /min within a 30–300 °C temperature under nitrogen flow 200 mL/min [5].
3	Fen Hwang et al.,	The disordering effect of hyoscyamine drugs on phospholipid membranes	They have reported the disordering activity of *Hyoscyamus niger* L on the fluidity of dipalmitoyl phatidylcholine liposomes has been studied by using DSC & the DSC result indicate that anisodamine, anisodine, atropine & scopolamine all increase fluidity of dipalmitoyl phosphatidylcholine liposomes but with different degree of efficiency at the rate of 5 °C /min within a 40–400 °C temperature under nitrogen flow 100mL/min [6].
4	Duy Toan Pham et al.,	Alpha mangostin loaded crosslinked silk fibroin-based nanoparticles for cancer chemotherapy	They have reported Alpha Mangostin loaded crosslinked silk fibroin based nano particles for cancer therapy by using DSC analytical method. Crosslinked FNP's (fibroin nano particles) exhibited higher drug entrapment efficiency (70%) drug loading (7%) than non-crosslinked FNP's this DSC method confirms that α-man-gostin was entrapped in FNP's in molecular dispersion form [7].
5	Maria Camilla Bergonzi et al.,	Studies on the interactions between some flavonols and cyclodextrins	They have reported complex interactions between some flavanols and cyclodextrins by using analytical methods like DSC in this the interactions of some natural flavanols with α, β, γ-cds have been studied. Mainly DSC used here to characterize the cd-flavanols system in solid state. Here the guest molecules like kaempferol & quercetin were difficult to interpreted because of their MP value at 284.3 °C and 326.5 °C respectively [8].
6	Darshan R Telange et al.,	Enhanced transdermal permeation and anti-inflammatory potential of phospholipids complex-loaded matrix film of umbelliferone: formulation development, physico-chemical and functional characterization	They have reported enhanced transdermal permeation and anti-inflammatory potential of phospholipids complex loaded matrix film of umbelliferon and its physiochemical parameters are determined by analytical method by using DSC and temperature range of 40 to 400 °C at a heating rate of 10 °C /min by using 50 mL/min nitrogen gas flow rate [9].
7	Ying Li et al.,	Comparative physicochemical characterization of phospholipids complex of puerarin formulated by conventional and supercritical methods	They have reported comparative physicochemical characterization of phospholipids complex of puerarin (phospholipid) formulated by conventional and supercritical methods and the solid state characterization of particles included DSC at temperature range of 25–230 °C and heating rate of 10 °C/min by DSC [10].
8	Felipe HugoA. Fernandes et al.,	Evaluation of compatibility between Schinopsis brasiliensis Engler extract and pharmaceutical excipients using analytical techniques associated with chemometric tools	They have reported evaluation of a united between *Schinopsis brasilinsis* extract and pharmaceutical excipients using analytical techniques associated with chemometric tools like DSC which gives better interpretation of united studies and that microcrystalline cellulose and experiment is conducted at temperature range from 25 °C to 40 °C and heating rate at 10 °C/min by using an instrument calorimeter model DSC Q20 [11].
9	Malay K Das et al.,	Design and evaluation of phyto-phospholipid complexes (phytosomes) of rutin for transdermal application	They have reported evaluation of Phyto-phospholipid complexes known as phytosomes of Rectin for transdermal application. By DSC method in which this analytical method confirms the Phyto-phospholipid complex formation. At temperature range of 50–300 °C and heat rate 10 °C/min under nitrogen gas flow condition by phosphatidylcholine and phytosomes (1:1) by model (TADE DSC) [12].
10	Zahra Hooresfand et al.,	Preparation and characterization of rutin-loaded nanophytosomes	They have reported preparation & characterization of Rectin loaded nanoparticles by using DSC method in which the physiochemical properties of prepared nano Phytosomes were evaluated by particle size analyses at temperature range of 30 °C to 300 °C and heating rate at 10 °C/min (Schimadzu DSC 60, Japan) [13].

Table 2 DSC interpretation on several herbal drugs (*continued*)

Sl. no	Author name	Title of the work	Description of analysis
11	Malgorzata Latos-Brazio et al.,	Effect of impregnation of biodegradable polyesters with polyphenols from *Cistus Linnaeus* and *Juglans regia Linnaeus* walnut green husk	They have reported method for combining the extraction of plant material and impregnation of biodegradable polymers. The exctract of selected plant material was used to impregnate polymers contained valuable polyphenolic compounds, as confirmed by FTIR and UV–Vis spectroscopy. After impregnation, the polymer samples showed greater thermal stability which was studied by DSC technique [14].
12	Clavdia-Crina Toma et al.,	Investigation of thermal behavior of nigellae sativae semen from different types of extracts	They have reported investigation of thermal behaviour of Nigella sativae semen from different types of extracts by using DSC in this method mainly used to study compatibility of the identify possible interactions between these components of drugs temperature range at 25 °C to 1000 °C and heating rate is at 10 °C/min [15].
13	Brahandutt et al.,	Formulation of eutectic mixture of curcumin with salicylic acid for improving its dissolution profile	They have reported formulation of eutectic mixture of curcumin with salicylic acid for its better dissolution profile by using DSC. DSC mainly used for characterization of eutectic mixture (2 mg). heated rate form 30–250 °C of atmospheric nitrogen gas at flow rate 60 m/min by using DSC instrument (DSC Q10V9.9 build 303, US). [16]
14	Vidyadhara Suryadevara et al.,	Studies on jackfruit seed starch as a novel natural superdisintegrant for the design and evaluation of irbesartan fast dissolving tablets	They have reported studies on Jack fruit seed starch as a novel natural super disintegrant for design and evaluation of irbesartan for dissolving tablets and DSC used here because based on dissolution, studies the DSC in performed on formation F5 and F8 to observe the drug-polymer interactions temperature range at 0 °C to 300 °C and a heating rate at 10 °C/min under nitrogen gas flow rate [17].
15	Dritan Hasa et al.,	Rationale of using Vinca minor Linne dry extract phytocomplex as a vincamine's oral bioavailability enhancer	They have reported rationale of Vinca minor linne dry extract phyto complex as a vincamine's oral bioavailability enhancer by using different analytical method among those DSC method used to characterize the chosen alkaloid enriched and standardized dry extract at heat rate 10°C/min and temperature range at 30 °C to 270 °C under static air atmosphere by equipment (Mod, TA 4000 equipped measuring cell DSC 20 meter) [18].
16	Abrar S Torky et al.,	Rationale of using *Vinca minor Linne* dry extract phytocomplex as a vincamine's oral bioavailability enhancer	They have reported novel skin penetrating berberine oleate complex capitalizing on hydrophobic ion pairing approach in which Brb-OL complex at heat rate 10°C /min and temperature range from 28 °C to 300 °C by using DSC (Differential Scanning Calorimetric) (Perkin Elmer, shellon, CT, USA) [19].
17	Prachi P Udapurkar et al.,	Development and charecterization of citrus limon-phospholipid complex as an effective phytoconstituent delivery system.	They have reported characterization of Citrus Limon phospholipid complex as an effective phyto constituent delivery system in which DSC is mainly used to characterize the phospholipid-SCL complex (Standardized Citrus Limon extract) by using DSC (Perkin Elmer, USA, JADE model) temperature range at 0 °C to 300 °C and a heating rate at 10 °C/min under nitrogen gas flow rate [20].
18	Geetha, Athira et al.,	Curcumin loaded cassava starch	They have reported the characterization of Curcumin loaded Cassava starch nanoparticles with improved cellular absorption by using analytical method in which DSC is mainly used to characterization of loaded nanoparticles by DSC (DSC ZZe, Mettler Schcoerfen Bach Switzerland) temperature range from 30°C to 300°C and heating rate at 20°C/min under nitrogen gas flow rate [21].
19	Pranjal Ray et al.,	Formulation and evaluation pf Phospholipid complex of Green Tea Polyphenol	They have reported evaluation and formulation of phospholipid complex of Green Tea polyphenol by using analytical method, in which DSC mainly used to EGCG-phospholipid complex characterization by using DSC (TA instruments, USA, model DSC Q10 V24.4Build 11b) at heating rate at 10 °C/min and temperature range from 0 °C to 400 °C in atmosphere of nitrogen. [22]
20	Xiaoyu Svi et al.,	Preparation, characterization and *in vivo* assessment of the bioavailability of glycyrrhizic acid microparticles by supercritical anti-solvent process	They have reported characterization and in vivo assessment of bioavailability of glycyrrhizin and microparticles by supercritical anti-solvent process by using analytical in which DSC (Setaram DSC131) used probes temperature range from 25°C to 300°C heating rate at 10 °C/min under nitrogen atmosphere [23].
21	Tapash Chakraborty et al.,	Oil of *Mesua ferrea* L. Seed as a promising pharmaceutical excipient in lipid based nanoformulation	They have reported oil of *Mesua Ferreal* L. seed as prominant pharmaceutical excipient in lipid based nano formulation by using different analytical methods in which DSC is used to check characterization and compatibility of oil general component of lipid nanoparticles it confirms no chemical interaction general component of lipid nanoparticles [24].
22	Sudarshan Singh et al.,	Physico-chemical and structural characterization of mucilage isolated from seeds of *Diospyros melonoxylon* Roxb	They have reported structural characterization and physiochemical of mucilage isolated from seeds of *Diospyros melanoxylon* Roxb. By using different analytical methods in which DSC used for the characterization and to identify glass transmission temperature of Gum (78 °C to 74 °C) at temperature range from 0 °C to 300 °C under nitrogen atmosphere and at heating rate at 10 °C/min by DSC (Mettler Toledo Star Sytem) [25].

DSC, differential scanning calorimetry.

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