Clinical Studies on Hawthorn (*Crataegus* spp.)

Cardiac Insufficiency

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Tauchert *et al*., 1999	Cardiac insufficiency NYHA Stage II	MC, O n=1,011 patients with cardiac insufficiency	24 weeks	80 mg tablet, 2x/day (160mg extract/day)	Crataegus Special Extract WS 1442	Hawthorn treatment associated with significant improvement in clinical symptoms (exercise tolerance, fatigue, palpitation, and exercise dyspnea); 83% decrease in ankle edema and nocturia; reduction in blood pressure, resting pulse rate, and the difference in the pressure/heart rate product (PHRP); improved ejection fraction and improvements in echocardiography.
Schmidt *et al*, 1998	Cardiac insufficiency NYHA Stages I and II	O, OL, MC n=3,664 with stable NYHA Stage I or II (average age 66.7 years)	8 weeks	300 mg tablet, 3x/day (900 mg extract/day)	Faros® 300 Dragées	After 8 weeks hawthorn treatment decreased average heart rate ($p<0.01$) from 79.9 to 75.2 beats per minute. Average pressure-rate product (PRP) scores reduced from 117 mm Hg per minute x 200 to 105.7 mm Hg per minute x 100 ($p<0.05$). Work tolerance, as determined by bicycle ergometry, increased from 93.5 to 109.7 watts (W) ($p<0.001$).
Loew *et al*., 1996	Cardiac insufficiency NYHA Stage I and II	OL, S n=1,476 patients with heart failure of NYHA Stages I and II	Evaluation after 1 month and 2 months	300 mg tablet, 3x/day (900 mg extract/day)	Faros® 300 Dragées	At end of surveillance period, symptom score dropped by a mean of 66.6% with NYHA Stage I patients largely symptom free. A subgroup of patients with borderline hypertension showed decreases in systolic and diastolic pressure (160 to 150 mm Hg and 89 to 85 mm Hg, respectively), a drop in heart rate from 89 to 79 beats per minute, and arrhythmias that were significantly reduced independent of heart failure.
Weikl *et al*., 1996	Cardiac insufficiency NYHA Stage II	DB, PC, MC n=136 patients with NYHA Stage II cardiac insufficiency (40–80 years)	2 months (after a 2 week run-in phase)	80 mg capsule, 2x/day (160 mg extract daily) vs. placebo	Crataegus Special Extract WS 1442	Hawthorn showed statistically significant superiority ($p=0.018$, U test, one-sided) in primary target parameter (change in pressure-rate/product [PRP] difference determined by systolic blood pressure x heart rate divided by 100) with a median decrease in PRP of 6.2 compared to +0.1 increase with placebo. Subjective complaints also decreased in hawthorn group ($p<0.05$).
Bödigheimer and Chase, 1994	Congestive heart failure, NYHA Stage II	R, DB, PC, MC n=85 patients with NYHA Stage II cardiac insufficiency	1 month	100 mg tablet, 3x/day (300 mg extract/day) vs. placebo	Faros® LI 132 Dragées	After 4 weeks there was a statistically insignificant trend towards improvement in clinical symptoms and in ergometric parameters, compared to placebo. The duration of use (only 4 weeks) and the relative low dosage (300 mg/day) may explain these results.
Förster *et al*., 1994	Congestive heart failure, NYHA Stage II	DB, PC n=72 patients with NYHA Stage II cardiac insufficiency	2 months	300 mg tablet, 3x/day (900 mg extract/day) vs. placebo	Faros® 300 Dragées	Oxygen uptake increased with hawthorn but not with placebo ($p<0.05$) based on ergospirometry. Time taken to reach anaerobic threshold during exercise increased by 30 seconds in hawthorn group and 2 seconds in placebo group. Hawthorn also showed significant improvements ($p<0.001$) in subjective complaint scores.
Schmidt *et al*., 1994	Cardiac insufficiency, NYHA Stage II	R, DB, PC, MC n=78 patients with NYHA Stage II cardiac insufficiency (men and women ages 45–73)	8 weeks with a 1 week washout period	One, 200 mg tablet, 3x/day (600 mg extract/day) vs. placebo	Faros® LI 132 Dragées containing 200mg Crataegus extract LI 132	Statistically significant ($p<0.001$) increase in exercise tolerance in hawthorn group by 28 watt (W) compared to 5 W in placebo group using ergometer bicycle (12.5 W). Hawthorn group showed significant reductions in systolic blood pressure ($p<0.05$) and heart rate ($p<0.01$). Subjective symptoms score also improved significantly ($p<0.001$).
Tauchert *et al*., 1994	Congestive heart failure NYHA Stage II	R, DB, MC, Cm n=132 patients with NYHA Stage II cardiac insufficiency	2 months (including a 1 week lower dosage introductory therapy period)	Three, 100 mg tablets, 3x/day (900 mg extract/day) vs. 12.5 mg, 3x/day of ACE inhibitor Captopril (37.5 mg/day)	Faros® LI 132 Dragées vs. captopril	None of the target parameters (ergometry, pressure-rate-product (PRP), score for 5 typical symptoms) showed significant differences between hawthorn and captopril groups. Both showed statistically significant increase ($p<0.001$) in maximum tolerated exercise performance, 83 to 97 watt (W) in hawthorn group and 83 to 99 W in captopril group. Both treatments reduced PRP and decreased incidence and severity of symptoms (shortness of breath; fatigue after exercise) by 50%.
Leuchtgens, 1993	Cardiac insufficiency, NYHA Stage II	R, DB, PC n=30 patients with NYHA Stage II cardiac insufficiency	2 months	80 mg capsule, 2x/day (160 mg extract/day) vs. placebo	Crataegus Special Extract WS 1442	Hawthorn showed statistically significant ($p<0.05$) improvements over placebo (hawthorn –11.6, placebo –4.9) in the pressure-rate-product (PRP) during exercise (systolic blood pressure x heart rate/100) using bicycle ergometer, in subjective complaints score (hawthorn –16.5, placebo –4, $p<0.05$), and in heart rate.

KEY: **C** – controlled, **CC** – case-control, **CH** – cohort, **CI** – confidence interval, **Cm** – comparison, **CO** – crossover, **CS** – cross-sectional, **DB** – double-blind, **E** – epidemiological, **LC** – longitudinal cohort, **MA** – meta-analysis, **MC** – multi-center, **n** – number of patients, **O** – open, **OB** – observational, **OL** – open label, **OR** – odds ratio, **P** – prospective, **PB** – patient-blind, **PC** – placebo-controlled, **PG** – parallel group, **PS** – pilot study, **R** – randomized, **RC** – reference-controlled, **RCS** – retrospective cross-sectional, **RS** - retrospective, **S** – surveillance, **SB** – single-blind, **SC** – single-center, **U** – uncontrolled, **UP** – unpublished, **VC** – vehicle-controlled.

Clinical Studies on Hawthorn (*Crataegus* spp.) (cont.)

Cardiac Insufficiency (cont.)

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Weikl and Noh, 1992	Congestive heart failure NYHA Stage II	OL n=20 patients with NYHA Stage II cardiac insufficiency and LVEF <55%	1 month	One to two, 80 mg capsules, 3x/day (240–480 mg extract/day)	Crataegutt® forte capsules	480 mg/day increased ejection fraction from 40.18% to 43.5% at rest and 41.51% to 46.56% during exercise using radionuclide angio-cardiography method. Slight decrease in blood pressure during rest and exercise. Treatment of 7 patients with 240 mg/day increased the LVEF from 29.8% to 30.45% based on nuclear resonance scanning method.
Eichstädt *et al*., 1989	Congestive heart failure, NYHA Stage II LVEF<55%	OL n=20 NYHA Stage II patients	1 month	Two, 80 mg tablet, 3x/day (480 mg extract/day)	Crataegus Special Extract WS 1442 (Crataegutt® forte)	Hawthorn improved exercise tolerance and cardiac performance as well as subjective symptoms using a bicycle ergometer. After 4 weeks, patients maximum exercise tolerance rose from 704 to 772 watts (W) x minute ($p<0.05$).
O'Conolly *et al*., 1986	Heart failure, NYHA Stage I or II	R, DB, PC, CO n=36 patients with Stage I or II cardiac insufficiency (average age 74 years)	6 weeks	60 mg tablet, 3x/day (180 mg extract/day)	Crataegutt® novo Filmtabletten	Patients treated with hawthorn had decreased heart rate and improved cardiac output under resting and exercise conditions. Pressure-rate-product (PRP) was significantly reduced and quality of life measurements significantly improved. Significant improvement in psychological assessment including reduction in anxiety ($p<0.0001$) and sleep behavior.
Hanak and Brückel, 1983	Coronary disease, NYHA Stage I and II	R, DB, PC n=60 patients with stable angina pectoris	3 weeks	60 mg tablet, 3x/day (180 mg extract/day) vs. placebo	Crataegutt® novo Filmtabletten	Electrocardiogram measures improved in hawthorn group, and blood flow and oxygen delivery to the heart muscle rose. Hawthorn patients also exercised for longer periods of time without an angina attack.
Iwamoto *et al*., 1981	Cardiac insufficiency, NYHA Stage II or III	DB, PC n=80 patients with NYHA Stage II cardiac insufficiency	6 weeks	Weeks 1–2: Two, 30 mg tablets 3x/day after meals (180 mg/day) Weeks 3–6; Two or three, 30 mg tablets 3x/day after meals (180 mg or 270 mg/day)	Crataegutt® Dragées 30 mg of an extract of *Crataegus monogyna* and *C. oxyacantha* per tablet	Compared to placebo, hawthorn group exhibited statistically significant improvement of cardiac function ($p<0.001$) and of subjective symptoms such as dyspnea and palpitations ($p<0.001$). No difference in improvements in ECG recordings between hawthorn and placebo groups.

KEY: C – controlled, **CC** – case-control, **CH** – cohort, **CI** – confidence interval, **Cm** – comparison, **CO** – crossover, **CS** – cross-sectional, **DB** – double-blind, **E** – epidemiological, **LC** – longitudinal cohort, **MA** – meta-analysis, **MC** – multi-center, **n** – number of patients, **O** – open, **OB** – observational, **OL** – open label, **OR** – odds ratio, **P** – prospective, **PB** – patient-blind, **PC** – placebo-controlled, **PG** – parallel group, **PS** – pilot study, **R** – randomized, **RC** – reference-controlled, **RCS** – retrospective cross-sectional, **RS** - retrospective, **S** – surveillance, **SB** – single-blind, **SC** – single-center, **U** – uncontrolled, **UP** – unpublished, **VC** – vehicle-controlled.